A STUDY ON NEURODEVELOPMENTAL OUTCOME OF INFANTS WITH HYPOXIC ISCHEMIC ENCEPHALOPATHYAT GOVERNMENT RAJAJI HOSPITAL MADURAI

DISSERTATION SUBMITTED FOR THE DEGREE OF

M.D BRANCH VII

(PAEDIATRIC MEDICINE)

MAY 2018

THE TAMILNADU

D.R M.G.R MEDICAL UNIVERSITY

CHENNAI, TAMILNADU

CERTIFICATE

This is to certify that the dissertation entitled **"A STUDY ON NEURODEVELOPMENTAL OUTCOME OF INFANTS WITH HYPOXIC ISCHEMIC ENCEPHALOPATHY"** is the bonafide work of **Dr. DURGA DEVI** in partial fulfilment of the university regulations of the Tamil Nadu Dr. M.G.R Medical University, Chennai, for M.D Degree Branch VII – PAEDIATRIC MEDICINE examination to be held in May 2018.

Place: Madurai

Date

Dr.MARUDHUPANDIYAN
M.S., FICS., FAIS.,
Dean,
Madurai Medical College,
Government Rajaji Hospital,
Madurai-625020

CERTIFICATE

This is to certify that the dissertation entitled "A **STUDY ON NEURODEVELOPMENTAL OUTCOME OF INFANTS WITH HYPOXIC ISCHEMIC ENCEPHALOPATHY**" is the bonafide work of **Dr.DURGA DEVI** in partial fulfilment of the university regulations of the Tamil Nadu Dr. M.G.R Medical University, Chennai, for M.D Degree Branch VII – PAEDIATRIC MEDICINE examination to be held in May 2018.

Place: Madurai
Date:

PROF. Dr. K. MATHIARASAN M.D., D.C.H
DIRECTOR
Institute of Child Health & Research Center,
Madurai Medical College,
Madurai – 625020

CERTIFICATE

This is to certify that the dissertation entitled **"A STUDY ON NEURODEVELOPMENTAL OUTCOME OF INFANTS WITH HYPOXIC ISCHEMIC ENCEPHALOPATHY"** is the bonafide work of **Dr. DURGA DEVI** in partial fulfilment of the university regulations of the Tamil Nadu Dr. M.G.R Medical University, Chennai, for M.D Degree Branch VII – PAEDIATRIC MEDICINE examination to be held in May 2018

Place: Madurai
Date:

PROF. Dr.S.BALASANKAR M.D., D.C.H.
PROFESSOR
Institute of Child Health & Research Center,
Madurai Medical College,
Madurai-625020

DECLARATION

I**, Dr. DURGA DEVI,** solemnly declare that the dissertation titled **"**A **STUDY ON NEURODEVELOPMENTAL OUTCOME OF INFANTS WITH HYPOXIC ISCHEMIC ENCEPHALOPATHY"** has been conducted by me at the Institute of Child Health and Research center, Madurai under the guidance and supervision of my unit Chief **PROF. DR. S. BALASANKAR M.D., D.C.H.**

This is submitted in part of fulfilment of the award of the degree of M.D (Pediatrics) for the May 2017 examination to be held under the Tamil Nadu Dr. M.G.R Medical University, Chennai. This has not been submitted previously by me for any Degree or Diploma from any other University.

PLACE: Madurai
Date:

Dr.DURGA DEVI S

ACKNOWLEDGEMENT

I sincerely thank **Prof.Dr.Marudhupandiyan,** the Dean, Government Rajaji Hospital and Madurai Medical College for permitting me to do this study.

It gives me immense pleasure to express my sincere thanks and gratitude to **Prof. Dr. K .Mathiarasan**, M.D, D.C.H, Director & Professor of Pediatrics for his able guidance, encouragement, valuable suggestions and support for this study.

I am greatly indebted to my chief **Prof.Dr. S. Balasankar** M.D, D.C.H, Professor of Pediatrics for his excellent guidance, able supervision, critical review, constant encouragement and full support rendered in every aspect of this study.

I express my sincere thanks to **Prof. Dr. Rajarajeshwaran, Prof.Dr.M.Kulandaivel**, **Prof.Dr.S.Shanmugasundaram, Prof Dr.Nandhini kuppusamy, Prof.Dr.N.Balasubramaniyan, Prof. Dr.N. Muthukumaran,** for their guidance and encouragement throughout the study.

I would like to thank the Registrar **Dr.D.Rajkumar M.D** for his valuable suggestions throughout the study.

I wish to express my sincere thanks to my guide and assistant professors **Dr .J .Balasubramanian M.D, D.C.H, DAA , Dr. B. Vanitha**

M.D, and Dr. R. Suresh M.D, for their invaluable guidance, support and suggestions at every stage of this study.

I also express my gratitude to all other assistant professors of our department and my fellow post graduates for their kind cooperation in carrying out this study.

I also thank the members of the Ethical Committee, Government Rajaji Hospital and Madurai Medical College, Madurai for allowing me to do this study.

I express my sincere thanks to my parents and my brother for their support throughout my study.

Last but not the least, I submit my heartfelt thanks to the children and their parents for extending full co –operation to complete my study successfully.

INDEX

INTRODUCTION

INTRODUCTION

Hypoxia refers to a decreased oxygenation to cells or organs. Ischemia refers to blood flow to cells or organs that is insufficient to maintain their normal function.

Hypoxic–ischemic encephalopathy (HIE) is an important cause of permanent damage to CNS tissues that may result in neonatal death or manifest later as cerebral palsy or developmental delay. Approximately 20-30% of infants with HIE die in the neonatal period, and 33-50% of survivors are left with permanent neurodevelopmental abnormalities (cerebral palsy, mental retardation). The greatest risk of adverse outcome is seen in infants with severe fetal acidosis (pH <6.7) (90% death / impairment) and a base deficit > 25 mmol/L (72% mortality).

Neonatal encephalopathy is a clinical term that describes an abnormal neurobehavioral state consisting of decreased level of consciousness and usually other signs of brain stem and / or motor dysfunction.

Hypoxic-ischemic encephalopathy is a term that describes encephalopathy with objective data to support a hypoxic-ischemic mechanism as the underlying cause for the encephalopathy.

The incidence of birth asphyxia is about 36.6 / 1000 live birth infants in Indian studies. According to World Health Organization (WHO), four to nine million cases of newborn asphyxia occur each year.

In spite of significant advances in monitoring technology, obstetric care and knowledge of fetal and neonatal pathologies, asphyxia still remains a significant cause of mortality and long- term morbidity. More than a million newborns who survive asphyxia at birth develop long-term problems such as cerebral palsy, mental retardation, hearing, speech, visual and learning disabilities.

An early intervention (EI) could improve neuro-developmental outcomes in survivors of birth asphyxia. Enrolment of high risk children and assessing their developmental status and planning for early intervention is of paramount importance. EI promotes child health, minimize developmental delays, cures existing disabilities, prevents functional deterioration, and promotes parent- child interaction.

By thorough neurodevelopmental assessment and follow up of asphyxiated babies, neurodevelopmental abnormalities can be identified early and subject for early intervention, thus long term morbidity can be minimized.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Ashaq et al[8] studied incidence and neurodevelopmental outcome of HIE babies. They found out the incidence was 2.2 % in their hospital. Neurodevelopmental delay was present in 31.2% of babies at the end of one year in HIE patients. Also found out low apgar score at 5 minutes and low pH were predictors of poor neurodevelopmental outcome.

Liliana et al studied factors associated with higher degree of severity in HIE and evaluate their outcomes. They found out that thompson score, abnormal aEEG at admission and at 48 hours, mechanical ventilation, acute renal failure, length of stay are associated with more severe HIE. They concludes that more severe HIE reflects worse outcomes and mild HIE is associated with normal outcome at 18 months of age.

Manxu et al [7] found out HIE infants with severe CT abnormality were associated with markedly lower psychomotor development when compared with normal infants and infants with mild CT abnormality.

Hence Cranial CT may be considered as reliable index to establish the prognosis of HIE.

Meena et al[6] found that early physiotherapy intervention improved the level of achievement of developmental domains in HIE infants.

Charlene et al[5] suggested to focus on cognitive skills and language development during assessment of 12 to 24 months of HIE survivors from their study.

Perez et al[4] found out children having HIE without major disability are increased risk for long term intellectual verbal / motor deficits. Hence long term follow up are necessary for early detection of neurodevelopmental impairment and early initiation of adequate therapies.

Samantha et al [3] studied vojta's system of kinesiological diagnosis to identify infants at risk for neurodevelopmental delay as early as 3 months of age.

Rabia G sezer[2] et al establish markers that can help in predicting prognosis of HIE infants with the help of cranial MRI and EEG. Cranial MRI has sensitivity and specificity of 83.3 % and 57.9 % respectively.

EEG with normal or mildly abnormal correlated with favourable outcome and moderate or severely abnormal EEG correlated with poor outcome.

Caroline et al[1] estimated that 23 % of neonatal deaths worldwide can be attributed to asphyxia. Also found out that countries with high NMR, death rate is 8 times more that of countries with low NMR.

The World Health Organization has defined birth asphyxia as "failure to initiate and sustain breathing at birth" and based on Apgar score as an Apgar score of <7 at one minute of life. The National Neonatal Perinatal Database (NNPD) 2000, used a similar definition for perinatal asphyxia and defined moderate asphyxia as slow gasping breathing or an Apgar score of 4-6 and severe asphyxia as no breathing or an Apgar score of 0-3 at one minute of life. The National Neonatology Forum of India has defined asphyxia as "gasping or ineffective breathing or lack of breathing at one minute of life".

The essential criteria for diagnosing perinatal asphyxia as outlined by ACOG & AAP are

- Prolonged metabolic or mixed acidemia (pH <7.0 on cord arterial blood sample)
- Persistence of an Apgar score of <3 for 5 min or longer
- Clinical neurologic manifestation as seizures, hypotonia, coma or HIE in the immediate neonatal period
- Evidence of multi-organ system dysfunction in the immediate neonatal period.

ETIOLOGY

In term new-borns, asphyxia can occur in the antepartum or intrapartum period as a result of impaired gas exchange across the placenta that leads to the inadequate provision of oxygen (02) and removal of carbon dioxide (C02) and hydrogen (H+) from the fetus.

Factors that increase the risk of perinatal asphyxia

1. Impairment of maternal oxygenation
2. Decreased blood flow from mother to placenta
3. Decreased blood flow from placenta to fetus
4. Impaired gas exchange across the placenta or at the fetal tissue Level
5. Increased fetal 0 2 requirement.

Etiologies of hypoxia-ischemia

1. Maternal factors: hypertension (acute or chronic), hypotension, Infection (including chorioamnionitis), hypoxia from pulmonary or cardiac disorders, diabetes, maternal vascular disease, and *inutero* exposure to cocaine.
2. Placental factors: abnormal placentation, abruption, infarction, fibrosis.
3. Uterine rupture.

4. Umbilical cord accidents: prolapse, entanglement, true knot, compression.
5. Abnormalities of umbilical vessels.
6. Fetal factors: anemia, infection, cardiomyopathy, hydrops, severe cardiac / circulatory insufficiency.
7. Neonatal factors: cyanotic congenital heart disease, persistent Pulmonary hypertension of the newborn (PPHN), cardiomyopathy, other forms of neonatal *cardio*genic and / or septic shock.

PATHOPHYSIOLOGY AND PATHOGENESIS

With **brief asphyxia,** there is a transient increase, followed by a decrease in heart rate (HR), mild elevation in blood pressure (BP), an increase in central venous pressure (CVP), and essentially no change in cardiac output (CO). This is accompanied by a redistribution of CO with an increased proportion going to the brain, heart, and adrenal glands **(diving reflex).** This diversion of blood flow to vital deep nuclear structures of the brain does not occur, hence results in the typical pattern of injury to the subcortical and brain stem nuclei.

With **prolonged asphyxia,** there can be a loss of pressure autoregulation and / or C02 vasoreactivity. This, in turn, may lead to further disturbances in cerebral perfusion, particularly when there is

cardiovascular involvement with hypotension and / or decreased cardiac output. A decrease in cerebral blood flow results in anaerobic metabolism and eventual cellular energy failure due to increased glucose utilization in the brain and a fall in the concentration of glycogen, phosphocreatine, and adenosine triphosphate (ATP). Prolonged asphyxia typically results in diffuse injury to both cortical and subcortical structures, with greater injury to neuronal populations particularly susceptible to HI insults.

Cellular dysfunction occurs as a result of diminished oxidative phosphorylation and ATP production. This energy failure impairs ion pump function, causing accumulation of intracellular Na +, cl-, H 20, and Ca2+; extracellular K+; and excitatory neurotransmitters (e.g., glutamate).

Impaired oxidative phosphorylation can occur during the primary HI insult(s) as well as during a secondary energy failure that usually occurs approximately 6 to 24 hours after the initiation of insult. Cell death can be either immediate or delayed, and either necrotic or apoptotic.

Immediate neuronal death (necrosis) can occur due to intracellular osmotic overload of Na + and Ca2+, from ion pump failure as above or excitatory neurotransmitters acting on inotropic receptors (such as the N-methyl-D-aspartate (NMDA) receptor.

Delayed neuronal death (apoptosis) occurs secondary to uncontrolled activation of enzymes and second messenger systems within the cell (e.g.Ca2+dependent lipases, proteases, and caspases); perturbation of mitochondrial respiratory electron chain transport; generation of free radicals and leukotrienes; generation of nitric oxide (NO) through NO synthase; and depletion of energy stores.

Reperfusion of previously ischemic tissue may cause further injury as it can promote the formation of excess reactive oxygen species (e.g., superoxide, hydrogen peroxide, hydroxyl, singlet oxygen), which can overwhelm the endogenous scavenger mechanisms, thereby causing damage to cellular lipids, proteins, and nucleic acids, as well as to the blood-brain barrier. This may result in an influx of neutrophils that, along with activated microglia, release injurious cytokines (e.g., interleukin 1 and tumor necrosis factor *α)*.

Topography of Brain Injury in Term Infants with HIE and Clinical Correlation			
AREA OF INJURY	**LOCATION OF INJURY**	**CLINICAL CORRELATE(S)**	**LONG-TERM SEQUELA(E)**
Selective neuronal necrosis	Entire neuraxis, deep cortical area, brainstem and pontosubicular	Stupor or coma Seizures Hypotonia Oculomotor abnormalities Suck/swallow abnormalities	Cognitive delay Cerebral palsy Dystonia Seizure disorder Ataxia Bulbar and pseudobulbar palsy
Parasagittal injury	Cortex and subcortical white matter Parasagittal regions, especially posterior	Proximal limb weakness Upper extremities affected more than lower extremities	Spastic quadriparesis Cognitive delay Visual and auditory processing difficulty
Focal ischemic necrosis	Cortex and subcortical white matter Vascular injury (usually middle cerebral artery distribution)	Unilateral findings. Seizures common and typically focal	Hemiparesis Seizures Cognitive delays
Periventricular injury	Injury to motor tracts, especially lower extremity	Bilateral and symmetric weakness in lower extremities More common in preterm infants	Spastic diplegia

NEUROLOGIC SIGNS

The clinical spectrum of HIE is described as mild, moderate, or Severe by sarnat anad sarnat staging of HIE.

SIGNS	STAGE 1 (mild)	STAGE 2 (moderate)	STAGE 3 (severe)
Level of consciousness	Hyperalert	Lethargic	Stuporous, coma
Muscle tone	Normal	Hypotonic	Flaccid
Posture	Normal	Flexion	Decerebrate
Tendon reflexes/clonus	Hyperactive	Hyperactive	Absent
Myoclonus	Present	Present	Absent
Moro reflex	Strong	Weak	Absent
Pupils	Mydriasis	Miosis	Unequal, poor light reflex
Seizures	None	Common	Decerebration
Electroencephalographic findings	Normal	Low voltage changing to seizure activity	Burst suppression to isoelectric
Duration	<24 hr if progresses; otherwise, may remain normal	24 hr-14 days	Days to weeks
Outcome	Good	Variable	Death, severe deficits

Encephalopathy

Newborns with HIE must have depressed consciousness by definition, whether mild, moderate, or severe. Mild encephalopathy can consist of an apparent hyperalert or jittery state, but the newborn does not respond appropriately to stimuli, and thus consciousness is abnormal. Moderate and severe encephalopathies are characterized by more impaired responses to stimuli such as light, touch, or even noxious stimuli. The background pattern detected by EEG or aEEG is useful for determining the severity of encephalopathy.

Brain stem and cranial nerve abnormalities

Newborns with HIE may have brain stem dysfunction, which may manifest as abnormal or absent brain stem reflexes, including pupillary, corneal, oculocephalic, cough, and gag reflexes. There can be abnormal eye movements such as dysconjugate gaze, gaze preference, ocular bobbing or other abnormal patterns of bilateral eye movements, and an absence of visual fixation or blink to light. Newborns may show facial weakness (usually symmetric) and have a weak or absent suck and swallow with poor feeding. They can have apnea or abnormal respiratory patterns.

Motor abnormalities

With greater severity of encephalopathy, there is generally greater hypotonia, weakness, and abnormal posture with lack of flexor tone, which is usually symmetric. With severe HIE, primitive reflexes such as the Moro or grasp reflex may be diminished. Over days to weeks, the initial hypotonia may evolve into spasticity and hyperreflexia if there is significant HI brain injury. Note that if a newborn shows significant hypertonia within the first day or so after birth, the HI insult may have occurred earlier in the antepartum and have already resulted in established HI brain injury.

Seizures occur in up to 50% of newborns with HIE, and usually start within 24 hours after the HI insult. Seizures indicate that the severity of encephalopathy is moderate or severe, not mild. Seizures may be subtle, tonic, or clonic. It can sometimes be difficult to differentiate seizures from jitteriness or clonus, although the latter two are usually suppressible with firm hold of the affected limb(s). Since seizures are often subclinical (electrographic only) and abnormal movements or posture may not be seizure, EEG remains the gold standard for diagnosing neonatal seizures, particularly in HIE. Seizures may compromise ventilation and oxygenation, those who are not receiving mechanical ventilation.

Increased intracranial pressure (ICP) resulting from diffuse cerebral edema in HIE often reflects extensive cerebral necrosis rather than swelling of intact cells and indicates a poor prognosis. Treatment to reduce ICP does not affect outcome.

MULTIORGAN DYSFUNCTION

Other organ systems in addition to the brain usually exhibit evidence of asphyxial damage. In a minority of cases (<15%), the brain may be the only organ exhibiting dysfunction following asphyxia. The kidney is the most common organ to be affected in the setting of perinatal asphyxia. The proximal tubule of the kidney is specially affected by decreased perfusion, leading to acute tubular necrosis with oliguria.

MULTIORGAN SYSTEMIC EFFECTS OF ASPHYXIA

SYSTEMS	EFFECT (S)
CNS	HIE, infarction, intracranial hemorrhage, seizures, cerebral edema, hypotonia, hypertonia
Cardiovascular	Myocardial ischemia, poor contractility, cardiac stunning, tricuspid insufficiency, hypotension
Pulmonary	Pulmonary hypertension, pulmonary hemorrhage, RDS
Renal	Acute tubular or cortical necrosis
Adrenal	Adrenal hemorrhage
Gastrointestinal	Perforation, ulceration with hemorrhage, necrosis
Metabolic	Inappropriate secretion of antidiuretic hormone, hyponatremia, hypoglycemia, hypocalcemia, myoglobinuria.
Integument	Subcutaneous fat necrosis
Hematology	Disseminated intravascular coagulation

LABORATORY EVALUATION OF ASPHYXIA

Cardiac evaluation

Cardiac troponin I (cTNI) and cardiac troponin T (cTnT), cardiac regulatory Proteins that control the calcium-mediated interaction of actin and myosin, are markers of myocardial damage. Normal values in the neonate are troponin I = 0 to 0.28 +/_ 0.42 JJ.µg/L and troponin T = 0 to 0.097 µg/L. Elevated levels of these proteins have been described in newborns with clinical and laboratory evidence of asphyxia.

An elevation of serum creatine kinase myocardial bound (CK-MB) fraction of >5% to 10% may indicate myocardial injury.

Neurologic markers of brain injury

Serum CK-BB may be increased in asphyxiated newborns within 12 hours of the insult, but has not been correlated with long-term neurodevelopmental outcome. CK-BB is also expressed in placenta, lungs, gastrointestinal tract, and kidneys. Other serum markers such as protein S-100, neuron specific enolase, and urine markers have been measured in newborns with asphyxia and HIE.

Renal evaluation

Blood urea nitrogen (BUN) and serum creatinine (Cr) may be elevated in perinatal asphyxia. Typically, elevation is noted 2 to 4 days after the insult. Fractional excretion (FE) of Na+ or renal failure index may help confirm renal insult. Urine levels of β2-microglobulin have been used as an indicator of proximal tubular dysfunction, although not routinely. This low molecular weight protein is freely filtered through the glomerulus and reabsorbed almost completely in the proximal tubule. Renal sonographic abnormalities correlate with the occurrence of oliguria.

BRAIN IMAGING

Cranial sonographic examination can demonstrate edema as loss of gray-white differentiation when severe, but is generally insensitive for the detection of HI brain injury, particularly in the first days after birth. It may be useful to rule out large intracranial hemorrhage, particularly since this may be a contraindication to therapeutic hypothermia.

Computed tomography (CT) may be used to detect cerebral edema, hemorrhage, and eventually HI brain injury. Because of the degree of radiation exposure, CT is only indicated if imaging is urgently needed to

determine clinical treatment and neither ultrasound nor MRI is available on an emergency basis.

Magnetic resonance imaging (MRI) Conventional T1- and T2-weighted MRI sequences are the best modality for determining the severity and extent of HI brain injury, but the injury is often not apparent on these sequences in the first days after the HI insult (unless the injury is older than suspected or very severe).These conventional sequences are best for the detection of brain injury after 7 to 10 days, and a scan as late as 14 days or older may be needed if there are clinical signs of HI brain injury without imaging correlates at an earlier time.

1. Diffusion-weighted imaging (DWI) can show abnormalities within hours of an HI insult that may be useful in the diagnosis of neonatal HIE and an early indicator of possible brain injury. However, DWI can both underestimate and overestimate the location and severity of HI brain injury, depending on the timing of the study. Early DWI scans will usually show restricted diffusion in brain regions affected by hypoxia-ischemia, although this does not inevitably mean that these regions are irreversibly injured. At 7 to 10 days of age, there is pseudonormalization of diffusion, so DWI can appear normal despite the presence of HI injury. After 7 to 10 days, diffusion is usually increased in regions of HI brain

injury. Thus, DWI data need to be interpreted carefully within the context of the history and clinical course of the newborn with HIE.

2. Proton magnetic resonance specttoscopy (MRS), also called *proton-MRS Or* 1 *H-MRS,* measures the relative concentrations of various metabolites in tissue. Elevated lactate, decreased N-acetylaspartate (NAA), and alterations of the ratios of these two metabolites in relation to choline or creatine can indicate HIE and help prognosticate neurologic outcome.
3. Susceptibility-weighted imaging may be useful for the detection of hemorrhage or hemorrhagic injury.
4. MR angiography or venography may occasionally be useful if there is suspicion of vascular anomalies, thromboembolic disease, or sinus venous thrombosis resulting in HI injury.

EEG is used both to detect and monitor seizure activity and also to define abnormal background patterns such as discontinuous burst suppression, low voltage, or isodectric patterns. When conventional 8- or 16-channd neonatal EEG is not readily available, amplitude-integrated EEG (aEEG) has been used to evaluate the background pattern, particularly when rapid assessment is needed for determination of treatment with therapeutic hypothermia. This method consists of a reduced montage with 1- or 2-channel EEG with parietal electrodes.

Although aEEG may detect some seizures, there are data showing that aEEG is insufficient to detect all seizures compared with conventional EEG, and that the quality of aEEG interpretation depends very much on the experience and expertise of the reader.

Developmental Therapy

Therapy Based on Passive Exercises

Out of the items assessed in the Amiel-Tison method, the angles give an important clue for the therapy and stimulation part of intervention. A limitation in angles indicates hypertonia and wide angle indicates hypotonia in most cases. In such instances, stimulation becomes effective only after normalizing the muscle tone. The purpose of passive therapy is essentially to reduce these deformities by constant effort of the mother in a playful manner. Home therapy based on Amiel-Tison passive angles is a simple concept which does not aim to hasten developmental milestones, but aims to prevent

- Mental subnormality by better mother-infant interaction
- Joint stiffening by repeated passive movements
- Contractures by repetitive passive movements
- Muscle wasting and fibrosis
- Helplessness in parents.

Therapy Based on Motor Milestones

Head Holding/Neck Control

- Stimulating the child to hold the head by carrying the child in an upright position by supporting the infant's head as and when possible.
- While playing and talking with the child, lift the child by supporting his upper arm and chest, thereby stimulating him to lift and hold his head.
- The child must be made to lie on his stomach and is guided on his elbow (a roll or round pillow can be used if necessary). Encourage the child to lift and hold his head by showing a colourful toy.
- Stimulate the child in prone position guiding on his hand on the surface, encourage the child to lift and hold his head and then rotate laterally showing a colorful toy.

Sitting

- Encourage the child to sit by putting him in an arm chair in a sitting position supporting him with pillows, as and when possible.
- While playing and talking with the child, encourage the child in sitting position with a wide base (thighs apart), supporting at the pelvis with a downward force.

- During play, the child can be encouraged in side-sitting position on both sides by supporting himself on the hand to the side which he is sitting.
- Guide the child to support on his hand and knees (four point kneeling / quadruped position) during play. A roll or pillow can be used if necessary. Then slowly guide him to sit on one of his sides supported by the same hand. Help the child to maintain this position for a while.
- Then guide him again on to his hands and knees and then gradually to side sitting on the other side.
- Baby walker can also be used to stimulate and improve sitting.

Standing

- Guide the child on to his both knees during play. Finally support him at the pelvis. If necessary, give support to the upper part of his body. Gradually the support can be withdrawn and the child can be made to support himself by holding on to a low stool. This position can be maintained by directing the child's attention to any play activity.
- From lying on the back position (supine position), stimulate the child to sit and gradually to the standing position during play time.

- Firstly, guide the child to his both knees supporting himself on a low stool with both hands. While directing his attention to a colourful toy through play, slowly help him to raise one leg so as to make him stand on one foot (leg straight), the other on the knee (half standing position) help the child to maintain this position while playing and talking with him. This position can be repeated on other side. Meanwhile depending on the child's ability, stimulate him to pull to standing position by himself, supporting on the stool.
- Encourage the child in standing position as and when possible, first with support then gradually withdrawing the support as per the child's ability. A baby walker will also severe the purpose of developing standing and walking skills.

AIMS AND OBJECTIVE

AIMS OF STUDY

- To assess the neurodevelopmental outcome of infants with Hypoxic Ischemic Encephalopathy.
- To assess the relationship between severity of Hypoxic

Ischemic Encephalopathy and neurodevelopmental outcome.

- To assess the neurodevelopmental outcome by DDST (Denver Developmental screening test) as screening tool and DASII (Development Assessment Scale for Indian Infants) as confirmatory.

SAMPLE SIZE : 150 infants

STUDY DESIGN : Hospital based Prospective analytical study

STUDY PERIOD : March 2016 - August 2017

STUDY POPULATION

Inclusion criteria : infants completed 37 weeks of gestation

- For inborn babies, Apgar score < 6 at 5 min or
- For outborn babies, history of asphyxia

1. h/o delayed first cry more than 5 minutes or
2. Need for positive pressure ventilation more than 1 minute.

Showing clinical signs of HIE as per sarnat and sarnat staging will be included.

Exclusion criteria

- Infants with Gestational age < 37 weeks,
- Perinatal infection,
- Congenital anomalies,
- Suspected metabolic disorders,
- Infants not been followed upto 1 year

MATERIALS AND METHODS

MATERIALS AND METHODOLOGY

After taking the informed written consent from the parent or guardian, the relevant information regarding pregnancy, delivery and neonatal period will be collected from the parents and neonatal records and recorded in a predesigned proforma. At enrollment detailed history and neurological examination will be done to detect neurological deficits and tone abnormalities. All infants with HIE will be screened in OPD at 3, 6, 9 and 12 months of age.

At each follow up they will be undergoing

1. Neurological examination using Amiel-Tison scoring at 3, 6, 9 and 12 months of age.
2. Neurodevelopmental assessment using DDST as screening tool at 3, 6, 9, 12 months and DASII as confirmatory test at the end of 1 yr and at any age for those who are found to be abnormal in using DDST.
3. Growth assessment (detailed anthropometry) and developmental milestones.
3. Nutrition Assessment (Breastfeeding or weaning)
4. Hearing assessment using OAE as screening test and Brainstem Evoked Response Audiometry(BERA) if warranted.
5. Vision assessment at first visit and subsequently VEP if warranted.

Neurological Evaluation

Amiel-Tison has provided us with a comprehensive system of neurological evaluation for the first year of life that gives us a framework for instituting physical therapy program. In the Amiel-Tison method of neurological evaluation presence of hypotonia is identifiedby measuring the following angles.

Adductor Angle: With the infant lying supine, the legs are extended and gently pulled as far apart as possible. The angle formed by the legs at this point is called the adductor angle. Asymmetry between the right and the left leg should be noted.

Heel to Ear: With the infant lying supine, the legs are held together and pressed as far as possible, towards the ear. The pelvis must not be lifted from the table. The angle is represented by the arc extending from the infant's heel to the table. Increased resistance on one side is an indication of asymmetry, but it might be difficult to apply equal pressure to both sides.

Popliteal Angle : The thighs are flexed laterally at the hip along both Sides of the abdomen. While holding the infant in this position, the examiner presses the lower leg as far as possible towards the thigh. The popliteal angle, which is formed by the calf and the thigh, is

estimated in both legs simultaneously. It is easier to apply equal pressure to both sides when examining the popliteal angle. Therefore, the estimation of asymmetry is more objective. Significant asymmetry is indicated by a difference of 10–20° between the right and left angles.

Dorsiflexion Angle of the Foot: The examiner holds the infant's leg straight and flexes the foot toward the leg. This is accomplished by applying pressure with the thumb to the sole of the foot. The dorsiflexion angle is formed by the dorsum of the foot and the anterior aspect of the leg.

Scarf Sign: The infant is held in a semi-reclining position, supported by the examiner's palm. At the same time, the examiner takes the infant's hand and pulls the arm as far as possible, across the chest towards the opposite shoulder. Four positions are possible in describing the position of the elbow in relationship to the umbilicus.

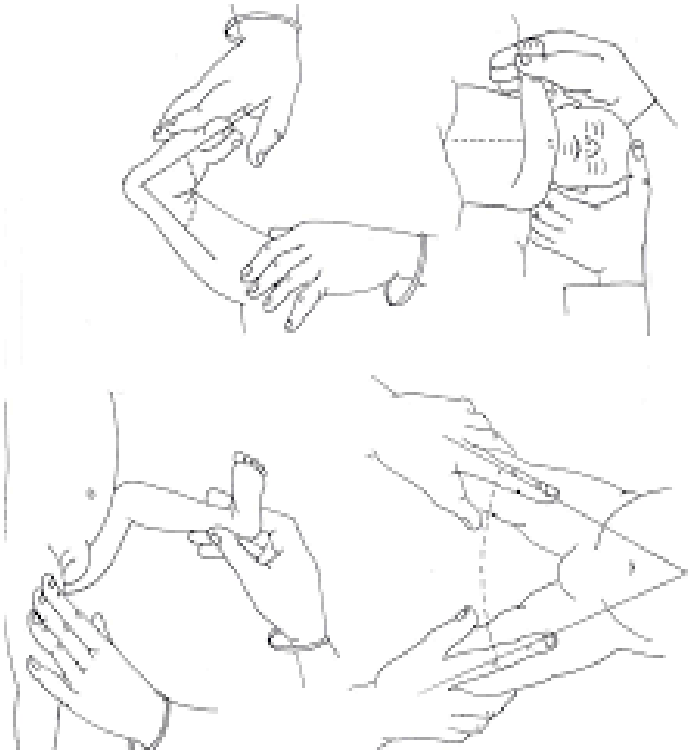


FIGURE SHOWING AMIEL TISON ANGLES

NEUROLOGICAL ASSESSMENT BY AMIEL TISON ANGLES

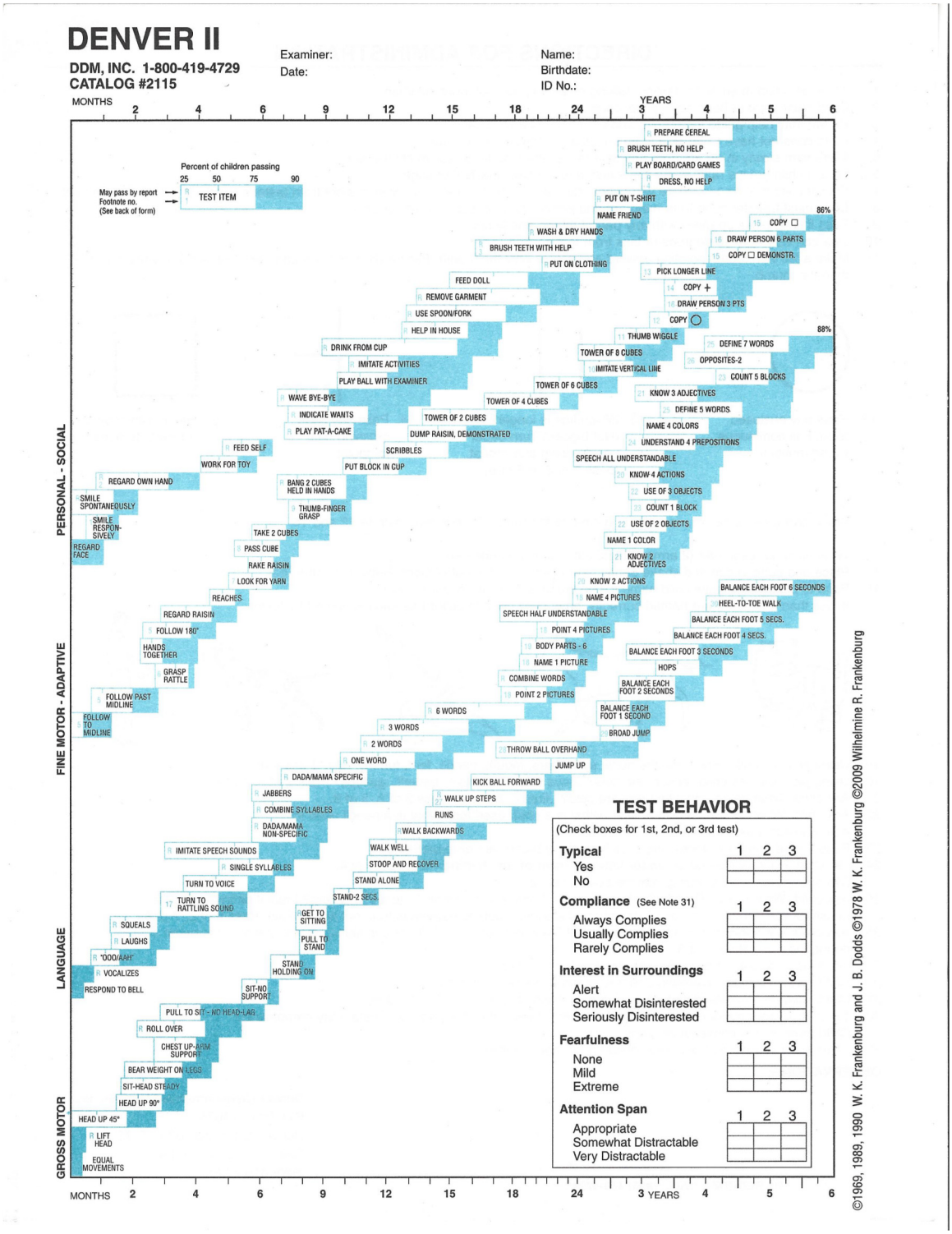
Age(month)	**Adductor angle**	**Popliteal angle**	**Dorsiflexion angle**	**Scarf sign**
0-3	40-80	80-100	60-70	Elbow not cross midline
4-6	70-120	90-120	”	Crosses midline
7-9	110-140	110-160	”	Goes beyond axillary line
10-12	140-160	150-170	”	

While doing DDST II the items intersected by and just adjacent to the age line will be tested. The items will be denoted as *P* for pass, F for failed, No for no opportunity, and R for refused to cooperate or attempt. The interpretation of the individual items will be made as follows:

a. Advanced : Child passes item that falls completely to the right of the age line.
b. Normal: Child fails or refuses an item that falls completely to the right of the age line / Child passes, fails, or refuses item on which the age line falls between the 25 th and 75 th percentile
c. Caution: Child fails or refuses item on which the age line falls between the 75 th and 90 th percentile.
d. Delayed: Child fails or refuses item that falls completely to the left of the age line.
e. No opportunity: Child has had no chance to perform the item (taken only for report items).

DDST II test overall interpretation will be done as

i. Normal: Child with no delays and a maximum of 1 caution.
ii. Suspect: Two or more cautions and /or one or more delays.
iii. Untestable: Refusal scores on 1 or more items completely to the left of age line or; more than one item intersected by the age line in the 75-90 th percentile area. These children will be rescreened again.


DENVER II
DDM, INC. 1-800-419-4729
CATALOG #2115
Examiner:
Date:
Name:
Birthdate:
ID No.:
MONTHS
YEARS
Percent of children passing
25 50 75 90
May pass by report
Footnote no.
(See back of form)
TEST ITEM
PERSONAL - SOCIAL
FINE MOTOR - ADAPTIVE
LANGUAGE
GROSS MOTOR
TEST BEHAVIOR
(Check boxes for 1st, 2nd, or 3rd test)
Typical
Yes
No
Compliance (See Note 31)
Always Complies
Usually Complies
Rarely Complies
Interest in Surroundings
Alert
Somewhat Disinterested
Seriously Disinterested
Fearfulness
None
Mild
Extreme
Attention Span
Appropriate
Somewhat Distractable
Very Distractable
1 2 3
©1969, 1989, 1990 W. K. Frankenburg and J. B. Dodds ©1978 W. K. Frankenburg ©2009 Wilhelmine R. Frankenburg

Infants with a normal neurological examination and normal DDST II will be considered as having normal neurodevelopmental outcome and those who have an abnormal neurological examination by DDST II will undergo DASII for further assessment. Those who has been untestable by DDST II will be reassessed after 2 weeks.

DEVELOPMENTAL ASSESSMENT SCALE FOR INDIAN INFANTS (DASII)

This is the gold standard test used for developmental evaluation, developed by Pramila Phatak, and is based on Bayley Scales of Infant

Development (BSID). Both mental development index and psychomotor development index can be calculated by DASII. The age placement of the item at the total score of the scale is noted as the child's developmental age. This gives child's total scores to his motor age (MoA) and mental age (MeA). The respective ages are used to calculate his motor and mental development quotients respectively by comparing them with his chronological age and multiplying it by 100.

(DMoQ = MoA/CA x 100 and DMeQ = MeA/CA x 100).

The composite development quotient (DQ) is derived as an average of DMoQ and DMeQ.

The test needs a special kit and cooperation of the child.

At 12 months of age all the babies will be assessed using Developmental Assessment Scales for Indian Infants (DASII). Abnormal neurodevelopmental outcome will be diagnosed if any one of the following abnormalities are to be identified-

1.MoQ or MeQ of less than 70% on DASII.

2.Hearing Loss.

3.Visual Impairment.

STATISTICAL ANALYSIS

The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer using SPSS v16 software. Using this software range, frequencies, percentages, means, standard deviations, chi square and p values were calculated.

Kruskul Wallis chi square test was used to test the significance of difference between quantitative variables. A p value less than 0.05 is taken to denote significant relationship.

RESULTS AND ANALYSIS

RESULTS AND ANALYSIS

Totally 150 infants were studied during the study period.

PROFILE OF STUDY PARTICIPANTS

TABLE 1 – GENDER DISTRIBUTION OF STUDY POPULATION

GENDER	N	%
Male	98	65.3%
Female	52	34.6%

Out of 150 infants, 98(65.3%) were male and 52 (34.6%) were female infants.

FIGURE 1 -GENDER DISTRIBUTION OF STUDY POPULATION

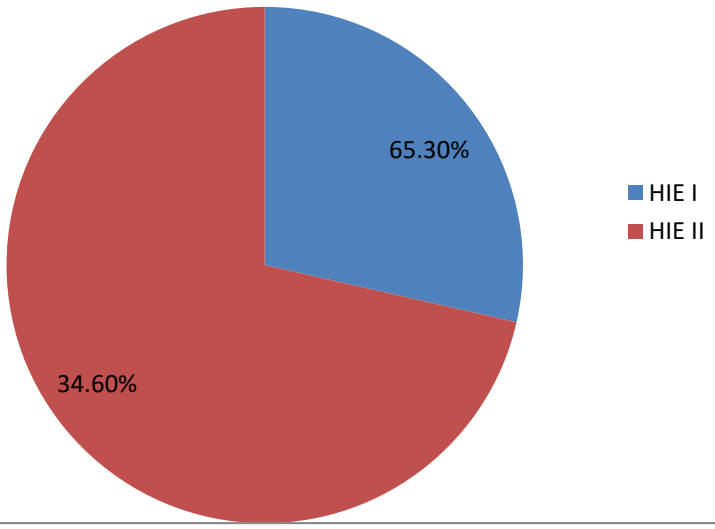


TABLE 2 - SEVERITY OF HIE - GENDERWISE

Variable N (%)			Diagnosis		
			HIE I **38 (25.3)**	**HIE II** **95 (63.3)**	**HIE III** **17 (11.3)**
Sex	Male	98 (65.3)	23 (60.5)	68 (71.6)	7 (41.2)
	Female	52 (34.6)	15(39.5)	27 (28.4)	10 (58.8)

Out of the 150 cases,38 (25.3 %) had HIE I, 95(63.3 %) had HIE II and 17(11.3%) cases had HIE III. Out of the 150 cases, 98 (65.3%) cases were males and 52 (34.6%) cases were females.

Out of the 38 HIE I cases, 23 (60.5 %) cases were males and 15 (39.5 %) cases were females.

Out of the 95 HIE II cases, 68 (71.6 %) cases were males and 27 (28.4%) cases were females.

Out of the 17 HIE III cases, 7 (41.2 %) cases were males and 10 (58.8 %) cases were females.

FIGURE 2-CASE DISTRIBUTION OF STAGES OF HIE IN STUDY POPULATION

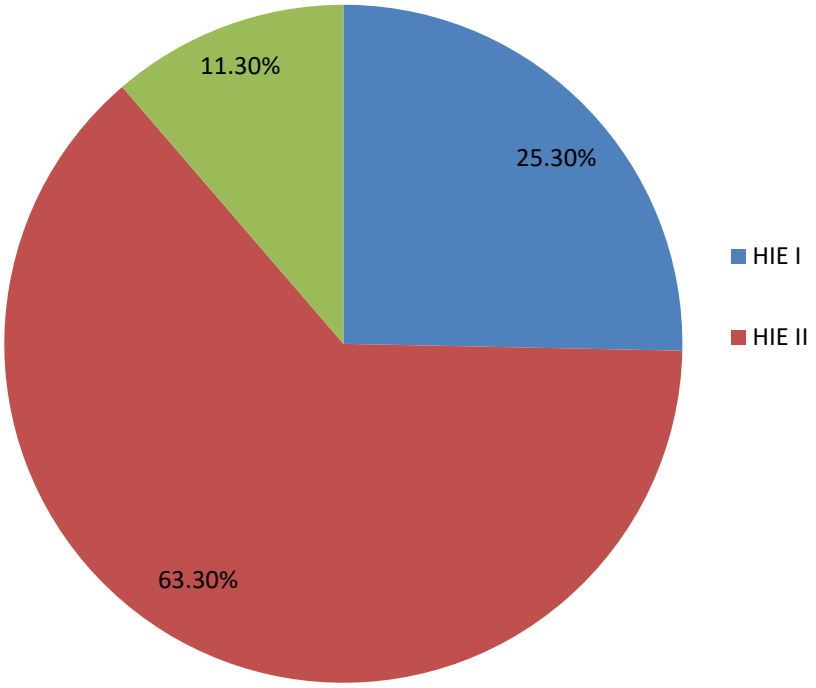


FIGURE 3 : SEVERITY OF HIE GENDERWISE

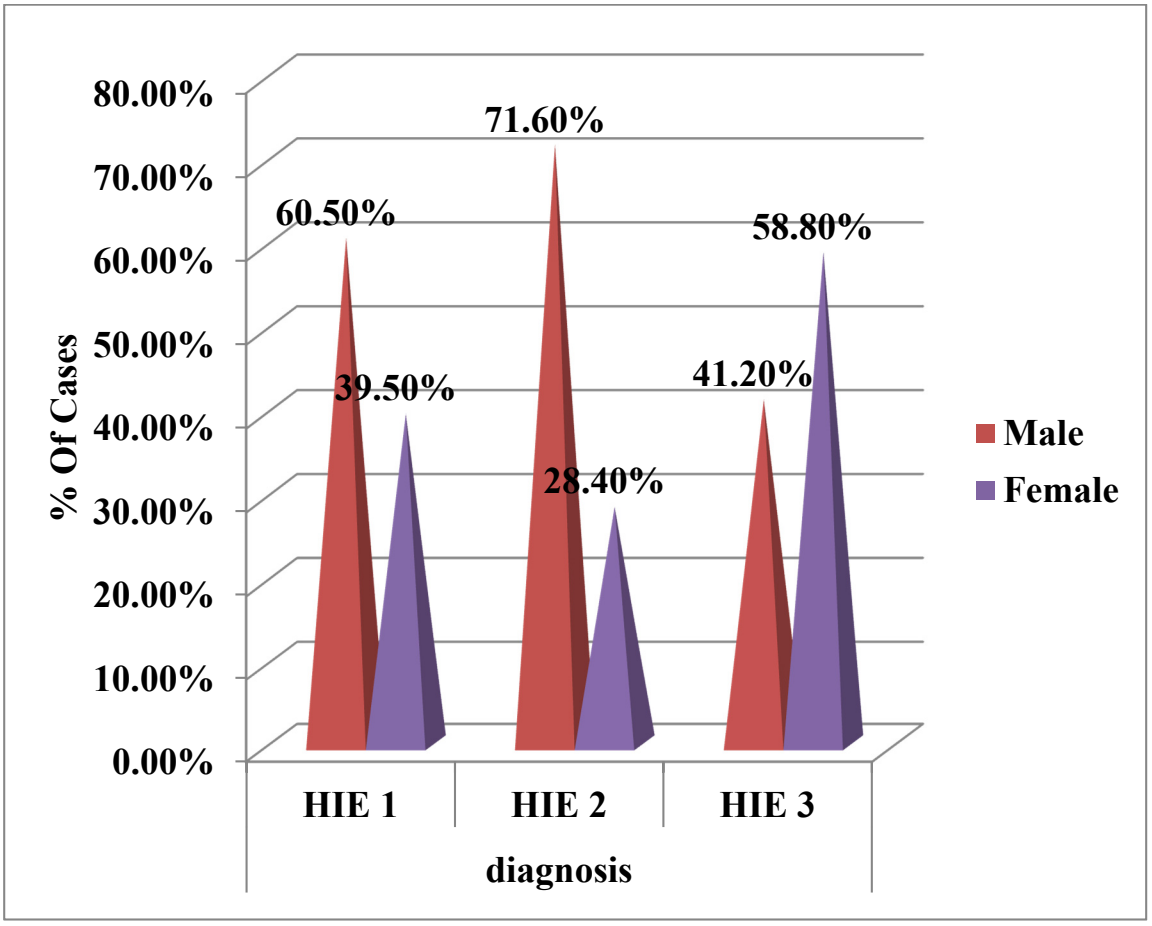


TABLE 3 – CASE DISTRIBUTION IN ALL STAGES OF HIE BASED ON ORDER OF BIRTH

Variable N (%)		Diagnosis		
		HIE I	HIE II	HIE III
Primi	100(66.6)	30 (78.9)	60 (63.2)	10 (58.8)
Multigravida	50(33.3)	8 (21.1)	35 (36.8)	7 (41.2)

Out of 150 HIE cases, 100 (66.6%) cases were delivered by primi gravida mothers and 50 (33.3%) cases were delivered by multigravida mothers.

Out of 38 HIE I cases, 30 (78.9%) cases were delivered by primi gravida mothers and 8 (21.1%) cases were delivered by multi gravida mothers.

Out of 95 HIE II cases, 60 (63.2 %) cases were delivered by primi gravida mothers and 35 (36.8%) cases were delivered by multi gravida mothers.

Out of 17 HIE III cases, 10 (58.8%) cases were delivered by primi gravida mothers and 8 (41.2%) cases were delivered by multi gravida mothers.

FIGURE 4 - CASE DISTRIBUTION IN ALL STAGES OF HIE BASED ON ORDER OF BIRTH

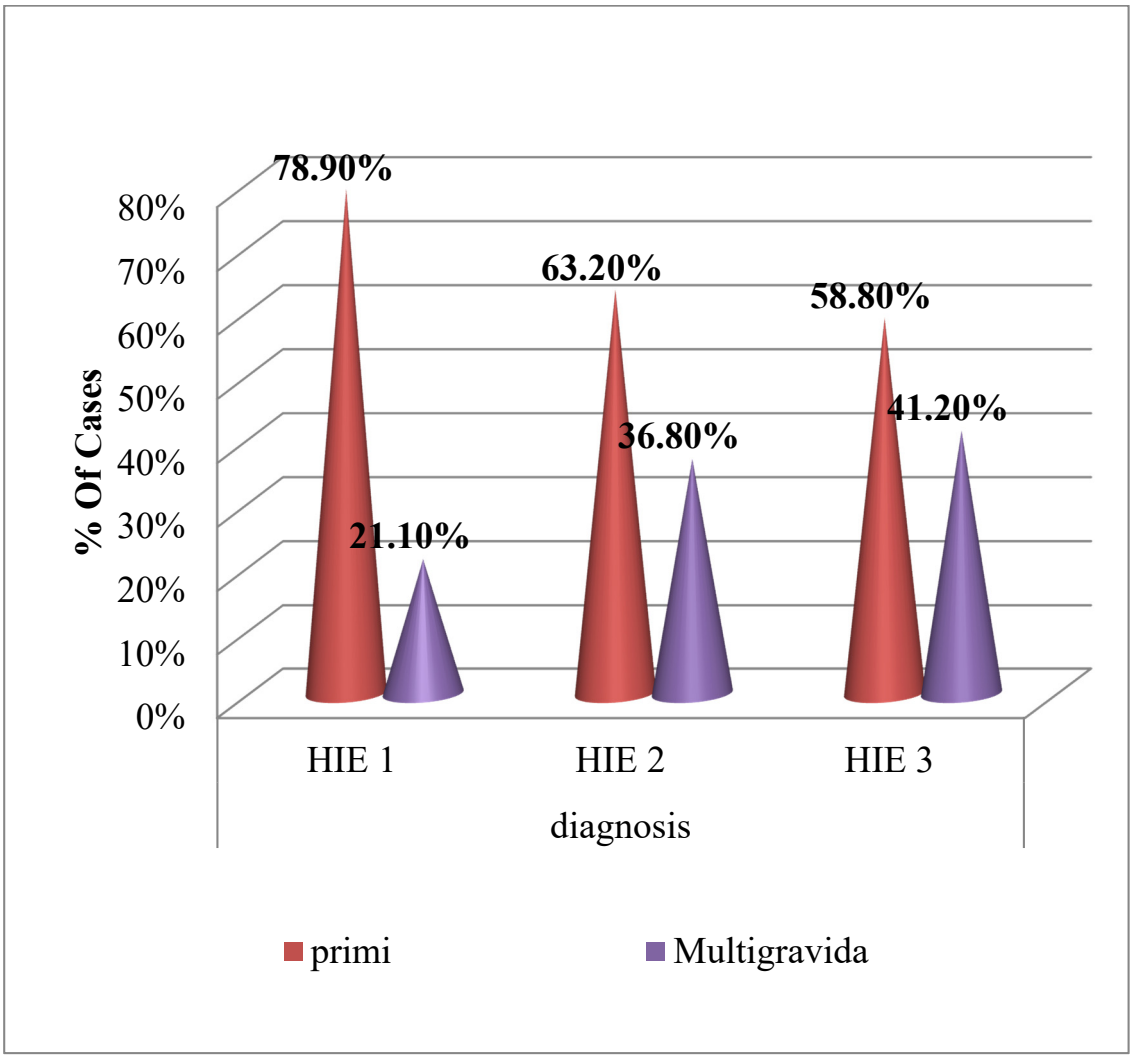


TABLE 4- CASE DISTRIBUTION IN ALL STAGES OF HIE BASED ON ANTENATAL RISK FACTORS

Variable N (%)			Diagnosis		
			HIE 1	HIE 2	HIE 3
Antenatal risk	No risk	92(61.3)	16(42.1)	62(65.3)	14(82.4)
	GDM	10(6.6)	5(13.2)	4 (4.2)	1(5.9)
	MAS	42(28)	14(36.8)	27(28.4)	1(5.9)
	PIH	6(4)	3(7.9)	2(2.1)	1(5.9)

Out of 150 HIE cases, 92(61.3%) had no antenatal risk factors. Other 58 cases had antenatal risk factors. Among them GDM 10 cases (6.6%), MAS 42 cases (28%), PIH 6 cases (4%).

Out of 38 HIE I cases,16 (42.1%) had no antenatal risk factors. Other 22 cases had antenatal risk factors. Among them GDM 5 cases(13.2%), MAS 14 cases (36.8 %), PIH 3 cases (7.9%).

Out of 95 HIE II cases,62 (65.3%) had no antenatal risk factors. Other 33 cases had antenatal risk factors. Among them GDM 4 cases(4.2%), MAS 27 cases (28.4 %), PIH 2 cases (2.1%).

Out of 17 HIE III cases,14 (82.4%) had no antenatal risk factors. Other 3 cases had antenatal risk factors. Among them GDM 1 case(5.9 %), MAS 1 case (5.9 %), PIH 1 case (5.9%).

FIGURE 5- CASE DISTRIBUTION OF ALL STAGES OF HIE BASED ON ANTENATAL RISK FACTORS

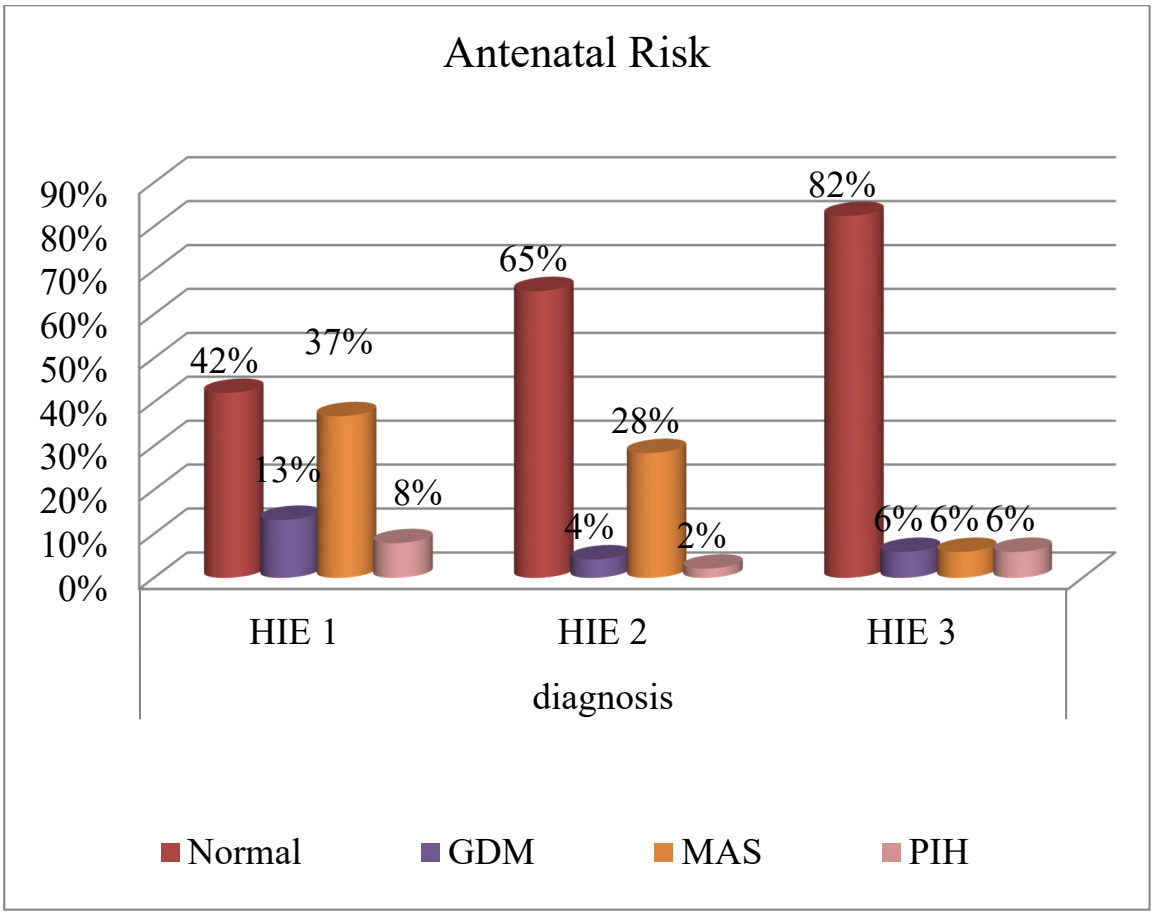


TABLE 5- CASE DISTRIBUTION OF ALL STAGES OF HIE BASED ON PLACE OF DELIVERY

Variable N(%)			Diagnosis		
			HIE I	HIE II	HIE III
O/I	Inborn	81(54)	31(81.6)	48 (50.5)	2 (11.8)
	Outborn	69 (46)	7 (18.4)	47 (49.5)	15 (88.2)

Out of 150 HIE cases, 81 (54%) cases were inborn and 69 (46%) cases were outborn.

Out of 38 HIE I cases, 31 (81.6%) cases were inborn and 7 (18.4%) cases were outborn.

Out of 95 HIE II cases, 48 (50.5%) cases were inborn and 47 (49.5 %) cases were outborn.

Out of 17 HIE III cases, 2 (11.8%) cases were inborn and 15 (88.2%) cases were outborn.

FIGURE 6 – CASE DISTRIBUTION OF ALL STAGES OF HIE BASED ON PLACE OF DELIVERY

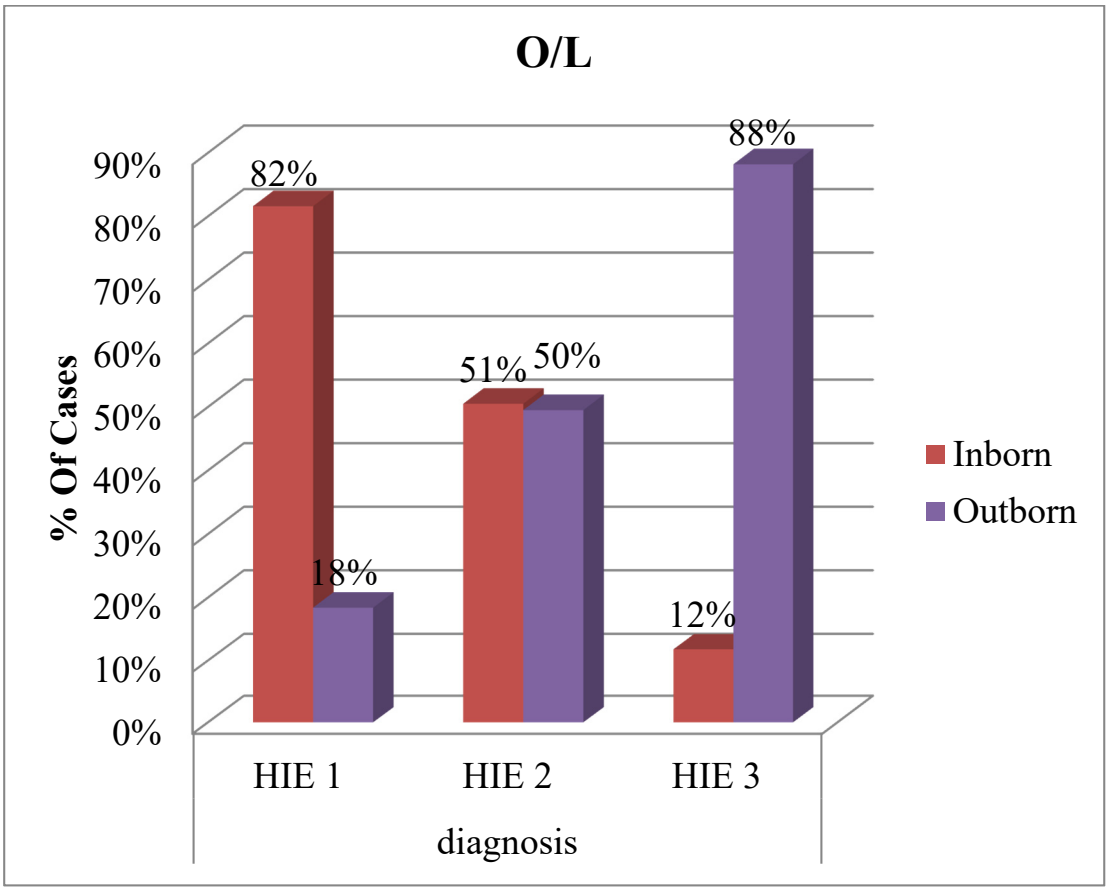


TABLE 5 - CASE DISTRIBUTION OF ALL STAGES OF HIE BASED ON MODE OF DELIVERY

Variable N(%)			Diagnosis		
			HIE I	HIE II	HIE III
Mode of delivery	Normal	111(74)	25 (65.8)	72(75.8)	14(82.4)
	AVD	9 (6)	2(5.3)	4(4.2)	3(17.6)
	LSCS	30(20)	11(28.9)	19(20)	0 (0)

Out of 150 total HIE cases, 111 (74%) cases were delivered by normal delivery, 9(6%) cases were delivered by AVD,30 (20%) cases were delivered by LSCS.

Out of 38 HIE I cases, 25 (65.8%) cases were delivered by normal delivery, 2 (5.3%) cases were delivered by AVD (assisted vaginal delivery),11 (28.9%) cases were delivered by LSCS

Out of 95 HIE II cases, 72 (75.8%) cases were delivered by normal delivery, 4 (4.2%) cases were delivered by assisted vaginal delivery,19 (20%) cases were delivered by LSCS.

Out of 17 HIE III cases, 14 (82.4 %) cases were delivered by normal delivery, 3 (17.6%) cases were delivered by assisted vaginal delivery.

FIGURE 7- CASE DISTRIBUTION OF ALL STAGES OF HIE BASED ON MODE OF DELIVERY

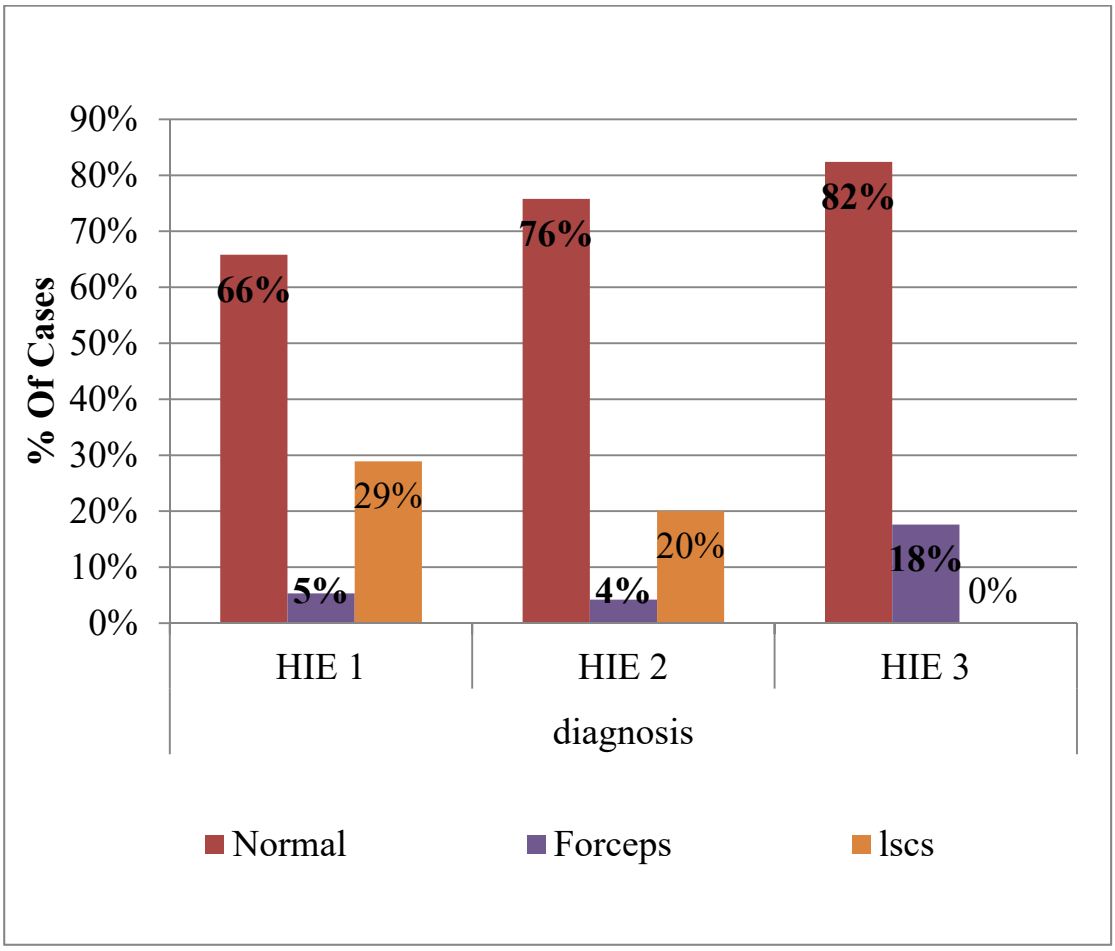


TABLE 7- CASE DISTRIBUTION IN ALL STAGES OF HIE BASED ON TYPES OF RESUSCITATION

Variable N (%)			Diagnosis		
			HIE 1	HIE 2	HIE 3
Resuscitation	No resuscitation	7(4.6)	1(2.6)	6(6.3)	0 (0)
	Tactile stimulation	25(16.6)	8 (21.1)	16(16.8)	1(5.9)
	Bag and Mask ventilation(BMV)	105(70)	25(65.8)	70(73.7)	10(58.8)
	Intubation	13(8.6)	4(10.5)	3(3.2)	6(35.3)

Out of 150 total HIE cases, 7 cases(4.6%) needed no resuscitation, 25 cases (16.6%) needed tactile stimulation, 105 cases (70%) needed BMV, 13 cases (8.6%) needed intubation.

Out of 38 HIE I cases, 1 case (2.6%)needed no resuscitation, 8 cases (21.1%) needed tactile stimulation, 25 cases (65.8%) needed BMV, 4 cases (10.5%) needed intubation .

Out of 95 HIE II cases, 6 cases (6.3%) needed no resuscitation, , 16 cases (16.8%) needed tactile stimulation, 70 cases (73.7%) needed BMV, 3 cases (3.2%) needed intubation .

Out of 17 HIE III cases, 1 case (5.9%) needed tactile stimulation, 10 cases (58.8%) needed BMV, 6 cases (35.3%) needed intubation.

FIGURE 8 - CASE DISTRIBUTION IN ALL STAGES OF HIE

BASED ON TYPES OF RESUCITATION

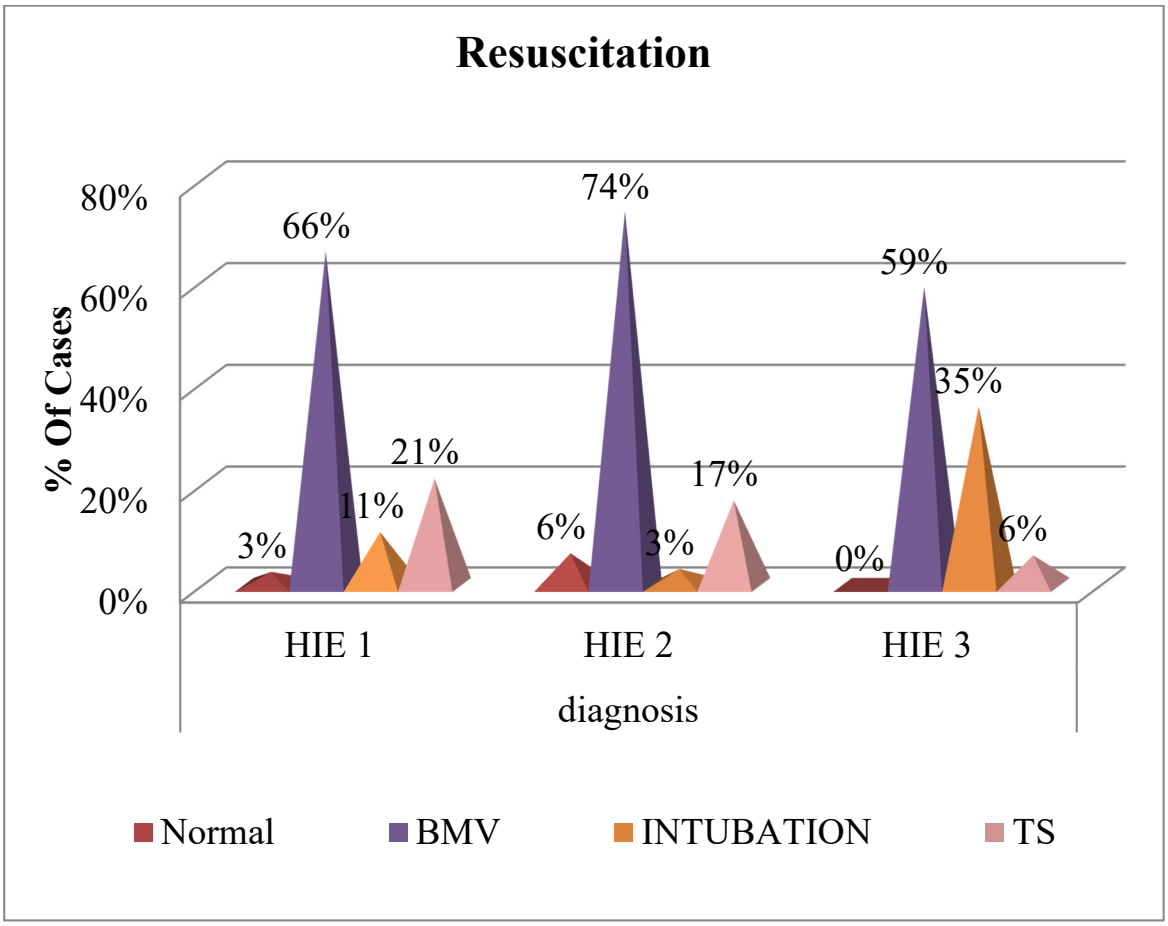


TABLE 8 – COMPLICATIONS OF HIE IN ALL STAGES

Variable N(%)			Diagnosis		
			HIE 1 (n-38)	HIE 2 (n-95)	HIE 3 (n-17)
NNC	Yes	107(71.3)	0 (0)	94(98.9)	13(76.5)
	No	43(28.6)	38(100)	1(1.1)	4(23.5)
Ventilation	Yes	38(25.3)	2 (5.3)	20(21.1)	16(94.1)
	No	112(74.6)	36(94.7)	75(78.9)	1(5.9)
Shock	Yes	16(10.6)	0(0)	2(2.1)	14(82.4)
	No	134(89.3)	38(100)	93(97.9)	3(17.6)
multi organ injury	Yes	15(10)	0(0)	3(3.2)	12(70.6)
	No	135(90)	38(100)	92(96.8)	5(29.4)
Sepsis	Yes	61(40.6)	11(28.9)	37(38.9)	13(76.5)
	No	89(59.3)	27(71.1)	58(61.1)	4(23.5)

Out of 150 total HIE cases,107 cases (71.3%) went in for neonatal convulsions, 38 cases (25.3%) needed ventilation, 16 cases (10.6%) went in for shock, 15 cases (10%) had multi organ injury, 61 cases (40.6%) had sepsis.

Out of 38 HIE I cases, 2(5.3 %) cases need ventilator support, 11 (28.9%) cases had sepsis. All HIE I cases not went in for convulsions, shock, multi organ injury.

Out of 95 HIE II cases, 94 (98.9%) cases went in for convulsions, 20(21.1%) cases need ventilator support, 2 (2.1%) cases went in for shock, 3(3.2%) cases had multi organ injury,37 (38.9%) cases had sepsis.

Out of 17 HIE III cases, 13 (76.5%) cases had convulsion, 16 cases (94.1%) need ventilator support, 14 (82.4%) cases went in for shock, 12 (70.6%) cases had multi organ dysfunction, 13 cases (76.5%) cases had sepsis.

TABLE 9 – ASSOCIATION BETWEEN LENGTH OF INFANTS AND STAGES OF HIE

Variable	Diagnosis	N	Mean	SD	p value
Length(cm)	HIE I	38	49	2.4	0.276
	HIE II	95	49	2.2	
	HIE III	17	48	3.1	

Among the 38 HIE I cases, mean value of length is 49 cm with standard deviation of 2.4.

Among the 95 HIE II cases, mean value of length is 49 cm with standard deviation of 2.2.

Among the 17 HIE III cases, mean value of length is 48 cm with standard deviation of 3.1.

A statistically significant association was not found between length and stages of HIE .(p value 0.276).

TABLE – 10 ASSOCIATION BETWEEN WEIGHT OF INFANTS AND STAGES OF HIE

Variable	Diagnosis	N	Mean	SD	p value
Weight(kg)	HIE I	38	3	0.52	0.532
	HIE II	95	3	0.52	
	HIE III	17	3	0.49	

The mean value of weight in HIE I and HIE II is 3 kg with standard deviation of 0.52.

The mean value of weight in HIE III is 3 kg with standard deviation of 0.49.

A statistically significant association was not found between weight and stages of HIE .(p value 0.532).

TABLE 11- NUMBER OF DAYS OF ADMISSION IN ALL STAGES OF HIE

NICU admission (no.of days)	N	Mean	Std. Deviation	p value
HIE 1	38	7.9	3.9	<0.001
HIE 2	95	11.2	4.9	
HIE 3	17	16.8	4.1	
Total	150	11	5.2	

The mean number of days of hospital stay in HIE I is 7.9 days with standard deviation of 3.9.

The mean number of days of hospital stay in HIE II is 11.2 days with standard deviation of 4.9.

The mean number of days of hospital stay in HIE III is 16.8 days with standard deviation of 4.1.

Over all mean hospital stay in all stages of HIE is 11 days with standard deviation of 5.2.

A significant statistical association was found between number of days of NICU stay and severity of HIE (p value <0.001)

TABLE 12- ASSOCIATION BETWEEN SEVERITY OF HIE AND VISION AT FIRST VISIT

Variable N(%)			Diagnosis			p value
			HIE 1	HIE 2	HIE 3	
Vision	Normal	139 (92.6)	36 (94.7)	89 (93.7)	14 (82.4)	0.218
	Abnormal	11 (7.3)	2 (5.3)	6 (6.3)	3 (17.6)	

During the first visit, visual examination was done in all HIE babies.

Among the total 150 HIE cases, 139 (92.6%) cases were found to be normal and 11 (7.3%) cases were found to be abnormal during the first visit.

Among the 38 HIE I babies, 36 (94.7%) cases were found to be normal and 2 (5.3%) cases were found to be abnormal.

Among the 95 HIE II babies, 89 (93.7%) cases were found to be normal and 6 (6.3%) cases were found to be abnormal.

Among the 17 HIE III babies, 14(82.4%) cases were found to be normal and 3 (17.6%) cases were found to be abnormal.

There was no significant statistical difference (P value 0.216) found between visual defect and severity of HIE during the first visit.

TABLE -13 ASSOCIATION BETWEEN SEVERITY OF HIE AND VISION DURING FOLLOW UP

Variable N(%)			HIE I	HIE II	HIE III	P-value
Vision	Normal	144(96)	38 (100)	89(93.7)	17(100)	0.164
	Abnormal	6 (4%)	0 (0)	6(6.3)	0(0)	

Among the 150 HIE cases, vision of 6 infants (4%) found to be abnormal, remaining 144 infants had normal vision during follow up visit.

Among the 38 HIE I cases, vision of 2 infants found to be abnormal in first visit, had been found to be normal during follow up visit.

Among the 95 HIE II cases, vision of 6 infants (6.3%) found to be abnormal in first and follow up visit. 89 cases found to be normal.

Among the 17 HIE III cases,vision of 3 cases found to be abnormal in the first visit, had been found to be normal during the follow up visit.

There was no significant statistical difference (P value 0.164) between vision and severity of HIE during the follow up visit.

TABLE 14 CASE DISTRIBUTION OF HEARING ABNORMALITY AMONG 3 STAGES OF HIE

Variables N(%)			Diagnosis		
			HIE 1	HIE 2	HIE 3
Hearing	Normal	119(79.3)	35 (92.1)	75 (78.9)	9 (52.9)
	Abnormal	31 (20.6)	3 (7.9)	20 (21.1)	8 (47.1)

Hearing initial assessment done in all HIE infants by using OAE screening.

Among the 150 HIE cases, 119 (79.3%) cases found to be normal and 31 cases (20.6%) found to be abnormal by OAE screening.

Among the 38 HIE I cases, 35(92.1%) cases found to be normal and 3 cases (7.9%) found to be abnormal.

Among the 95 HIE II cases, 75 (78.9%) cases found to be normal and 20 (21.1%) cases found to be abnormal.

Among the 17 HIE III cases, 9(52.9%) cases found to be normal and 8 (47.1%) cases found to be abnormal.

TABLE 15- RESULTS OF BERA FOR HIE INFANTS WITH ABNORMAL HEARING SCREENING

BERA	HIE I	HIE II	HIE III
Normal	3 (100)	20 (100)	7 (87.5)
Abnormal	0 (0)	0 (0)	1 (12.5)

BERA was done in HIE infants with abnormal hearing screening.

Results were 3 cases of HIE I with abnormal hearing screening, found to had normal BERA (100%).

20 cases of HIE II with abnormal hearing screening found to had normal BERA (100%).

Among 8 cases of HIE III with abnormal hearing screening, 7 cases (87.5%) had normal BERA and 1 case (12.5%) had abnormal BERA.

TABLE 15- ASSOCIATION BETWEEN TONE ABNORMALITY AND SEVERITY OF HIE DURING FIRST VISIT

Variable		N (%)	Diagnosis			pValue
			HIE I	HIE II	HIE III	
Tone	Normal	118(78.6)	37(97.4)	78 (82.1)	3(17.6)	<0.001
	Abnormal	32 (21.3)	1 (2.6)	17 (17.9)	14 (82.4)	

Among the 150 HIE cases, 118 cases (78.6%) had normal tone and 32 cases (21.3%) had abnormal tone.

Among the 38 HIE I cases, 37 cases (97.4%) had normal tone and 1 case (2.6 %) had abnormal tone.

Among the 95 HIE II cases, 78 cases (82.1%) had normal tone and 1 cases(17.9 %) had abnormal tone.

Among the 17 HIE III cases, 3 cases (17.6%) had normal tone and 14 cases (82.4 %) had abnormal tone.

A significant statistical difference (p value< 0.001) was found between tone abnormality and severity of HIE.

TABLE 16 - ASSOCIATION BETWEEN TONE AND SEVERITY OF HIE DURING FOLLOW UP USING AMIEL TISON ANGLE

Tone N (%)			HIE I	HIE II	HIE III	p value
3 month	Normal	121 (80.6)	37 (97.4)	80 (84.2)	4 (23.5)	0.001
	Abnormal	29 (19.3)	1 (2.6)	15 (15.8)	13 (76.5)	
6 month	Normal	118 (78.6)	37 (97.4)	77 (81.1)	4 (23.5)	0.002
	Abnormal	32 (21.3)	1 (2.6)	18 (18.9)	13 (76.5)	
9 month	Normal	119 (79.3)	37 (97.4)	78 (82.1)	4 (23.5)	<0.001
	Abnormal	31 (20.6)	1 (2.6)	17 (17.9)	13 (76.5)	
12 month	Normal	119 (79.3)	37 (97.4)	78 (82.1)	4 (23.5)	<0.001
	Abnormal	31 (20.6)	1 (2.6)	17 (17.9)	13 (76.5)	

During 3rd month follow up,

Among the 38 HIE I cases, 37 cases (97.4%) were found to be normal and 1 case (2.6%) found to be abnormal.

Among the 95 HIE II cases, 80 cases (84.2%) were found to be normal and 15 cases (15.8 %) found to be abnormal.

Among the 17 HIE III cases, 4 cases(23.5%) were found to be normal and 13 cases (76.5%) found to be abnormal.

A significant statistical difference (P value 0.001) was found between tone abnormality and severity of HIE during 3rd month follow up.

During 6th month follow up,

Among the 38 HIE I cases, 37 cases (97.4%) were found to be normal and 1 case (2.6%) found to be abnormal.

Among the 95 HIE II cases, 77 cases (81.1%) were found to be normal and 18 cases (18.9 %) found to be abnormal.

Among the 17 HIE III cases, 4 cases(23.5%), were found to be normal and 13 cases (76.5%) found to be abnormal.

A significant statistical difference (P value 0.001) was found between tone abnormality and severity of HIE during 6th month follow up.

During 9th month follow up,

Same findings were seen in HIE I AND HIE III cases.

Among the 95 HIE II cases,78 cases (82.1%) were found to be normal and 17 cases (17.9%) were found to be abnormal.

A significant statistical difference (P value 0.001) was found between tone abnormality and severity of HIE during 9th month follow up.

During 12thmonth follow up,

Same findings of tone abnormality were seen in HIE I, HIE II and HIE III cases.

A significant statistical difference (P value 0.001) was found between tone abnormality and severity of HIE during 12th month follow up.

TABLE 17- ASSOCIATION BETWEEN HEAD CIRCUMFERENCE AND SEVERITY OF HIE DURING FIRST VISIT

Variable		N	Mean	Std. Deviation	95% Confidence Interval for Mean		P-Value
					Lower Bound	Upper Bound	
HC (cm)	HIE 1	38	34.9737	1.29504	34.5480	35.3994	0.877
	HIE 2	95	34.8526	1.32519	34.5827	35.1226	
	HIE 3	17	34.8118	1.63052	33.9734	35.6501	

During the first visit,

Among the 38 HIE I cases, the mean head circumference was 34.9 cm with standard deviation of 1.29.

Among the 95 HIE II cases, the mean head circumference was 34.8 cm with standard deviation of 1.32.

Among the 17 HIE III cases, the mean head circumference was 34.8 cm with standard deviation of 1.63.

A significant statistical difference (P value 0.877) was not found between head circumference and severity of HIE during first visit.

TABLE 18 – ASSOCIATION BETWEEN HEAD CIRCUMFERENCE AND SEVERITY OF HIE DURING FOLLOW UP

Head circumference (cm)		N	Mean	Std. Deviation	95% Confidence Interval for Mean		pValue
					Lower Bound	Upper Bound	
3 month	HIE 1	38	38.4286	1.63780	36.9139	39.9433	0.894
	HIE 2	95	38.2455	1.73582	37.4758	39.0151	
	HIE 3	17	37.9600	1.51921	36.0737	39.8463	
6 month	HIE 1	38	41.3368	1.57350	40.8196	41.8540	<0.001
	HIE 2	95	40.3084	2.14345	39.8718	40.7451	
	HIE 3	17	38.5706	2.49944	37.2855	39.8557	
9 month	HIE 1	38	42.8368	1.32674	42.4008	43.2729	<0.001
	HIE 2	95	41.8274	2.22115	41.3749	42.2798	
	HIE 3	17	39.9294	2.86308	38.4574	41.4015	
12 month	HIE 1	38	44.3079	1.43854	43.8351	44.7807	<0.001
	HIE 2	95	43.2684	2.34186	42.7914	43.7455	
	HIE 3	17	41.2118	3.57996	39.3711	43.0524	

During the 3rd month follow up,

Among the 38 HIE I cases, the mean head circumference was 38.4 cm with standard deviation of 1.63.

Among the 95 HIE II cases, the mean head circumference was 38.2cm with standard deviation of 1.73.

Among the 17 HIE III cases, the mean head circumference was 37.9cm with standard deviation of 1.51.

A significant statistical difference (P value 0.894) was not found between head circumference and severity of HIE during 3rd month follow up.

During the 6th month follow up,

Among the 38 HIE I cases, the mean head circumference was 41.3cm with standard deviation of 1.57.

Among the 95 HIE II cases, the mean head circumference was 40.3cm with standard deviation of 2.14.

Among the 17 HIE III cases, the mean head circumference was 38.5cm with standard deviation of 2.49.

A significant statistical difference(p value 0.001) was found between decrease in head circumference and severity of HIE during 6th month follow up.

During the 9th month follow up,

Among the 38 HIE I cases, the mean head circumference was 42.8cm with standard deviation of 1.32.

Among the 95 HIE II cases, the mean head circumference was 41.8cm with standard deviation of 2.22.

Among the 17 HIE III cases, the mean head circumference was 39.9cm with standard deviation of 2.86.

A significant statistical difference(p value 0.001) was found between decrease in head circumference and severity of HIE during 9th month follow up.

During the 12th month follow up,

Among the 38 HIE I cases, the mean head circumference was 44.3cm with standard deviation of 1.43.

Among the 95 HIE II cases, the mean head circumference was 43.2 cm with standard deviation of 2.34.

Among the 17 HIE III cases, the mean head circumference was 41.2cm with standard deviation of 3.57

A significant statistical difference (P value 0.001) was found between decrease in head circumference and severity of HIE during 12th month follow up.

TABLE 19 – ASSOCIATION BETWEEN DDST AND SEVERITY OF HIE DURING FOLLOW UP

Variable N(%)			Diagnosis			p value
			HIE 1	HIE 2	HIE 3	
DDST (3rd month)	Normal	110 (73.3)	36 (94.7)	70 (73.7)	4 (23.5)	<0.001
	Abnormal	40 (26.6)	2 (5.3)	25 (26.3)	13 (76.5)	
DDST (6th month)	Normal	95 (63.3)	33 (86.8)	62 (65.3)	0 (0)	<0.001
	Abnormal	55 (36.6)	5 (13.2)	33 (34.7)	17 (100)	
DDST (9th month)	Normal	86 (57.3)	32 (84.2)	54 (56.8)	0 (0)	0.004
	Abnormal	64 (42.6)	6 (15.8)	41 (43.2)	17 (100)	

As per DDST at 3rd month follow up,

Among the 150 HIE cases, 110 cases(73.3%) found to be normal and 40 cases (26.6%) found to be abnormal.

Among the 38 HIE I cases, 36 cases(94.7%) found to be normal and 2 cases (5.3%) found to be abnormal

Among the 95 HIE II cases, 70 cases(73.7%) found to be normal and 25 cases (26.3%) found to be abnormal.

Among the 17 HIE III cases, 4 cases(23.5%) found to be normal and 13 cases (76.5%) found to be abnormal.

As per DDST at 6rd month follow up,

Among the 150 HIE cases, 95 cases(63.3%) found to be normal and 55 cases (36.6%) found to be abnormal.

Among the 38 HIE I cases, 33 cases(86.8%) found to be normal and 5 cases (13.2%) found to be abnormal.

Among the 95 HIE II cases, 62 cases(65.3%) found to be normal and 33 cases (34.7%) found to be abnormal.

Among the 17 HIE III cases, 17 cases (100%) found to be abnormal.

As per DDST at 9th month follow up,

Among the 150 HIE cases, 86 cases(57.3%) found to be normal and 64 cases (42.6%) found to be abnormal.

Among the 38 HIE I cases, 32 cases(84.2%) found to be normal and 6 cases (15.8%) found to be abnormal

Among the 95 HIE II cases, 54 cases(56.8%) found to be normal and 41 cases (43.2 %) found to be abnormal.

Among the 17 HIE III cases, 17cases (100%) found to be abnormal.

A significant statistical association (P value 0.004) was found between denver developmental screening test and severity of HIE during 3^{rd},6^{th} ,9^{th} month follow up.

TABLE 20 – ASSOCIATION BETWEEN SEVERITY OF HIE AND DEVELOPMENTAL DELAY IN DASII AT THE END OF FOLLOW UP (12 MONTH)

Variable			Diagnosis			pValue
			HIE 1	HIE 2	HIE 3	
DASII	Normal	81 (54)	32 (84.2)	48 (50.5)	1 (5.9)	<0.001
	Abnormal	69 (46)	6 (15.8)	47 (49.5)	16 (94.1)	

At the end of follow up (12th month)

Among the 38 HIE I cases, 32 cases(84.2%) found to be normal and 2 cases(15.8%) found to be abnormal.

Among the 95 HIE II cases, 48 cases(50.5%) found to be normal and 47 cases(49.5%) found to be abnormal.

Among the 17 HIE III cases, 1 case (5.9 %) found to be normal and 16 cases(94.1 %) found to be abnormal.

A significant statistical association (P value 0.001) was found between severity of HIE and developmental delay as per DASII at the end of 1 year follow up.

FIGURE 9- ASSOCIATION BETWEEN SEVERITY OF HIE AND DEVELOPMENTAL DELAY IN DASII AT THE END OF FOLLOW UP (12 MONTH)

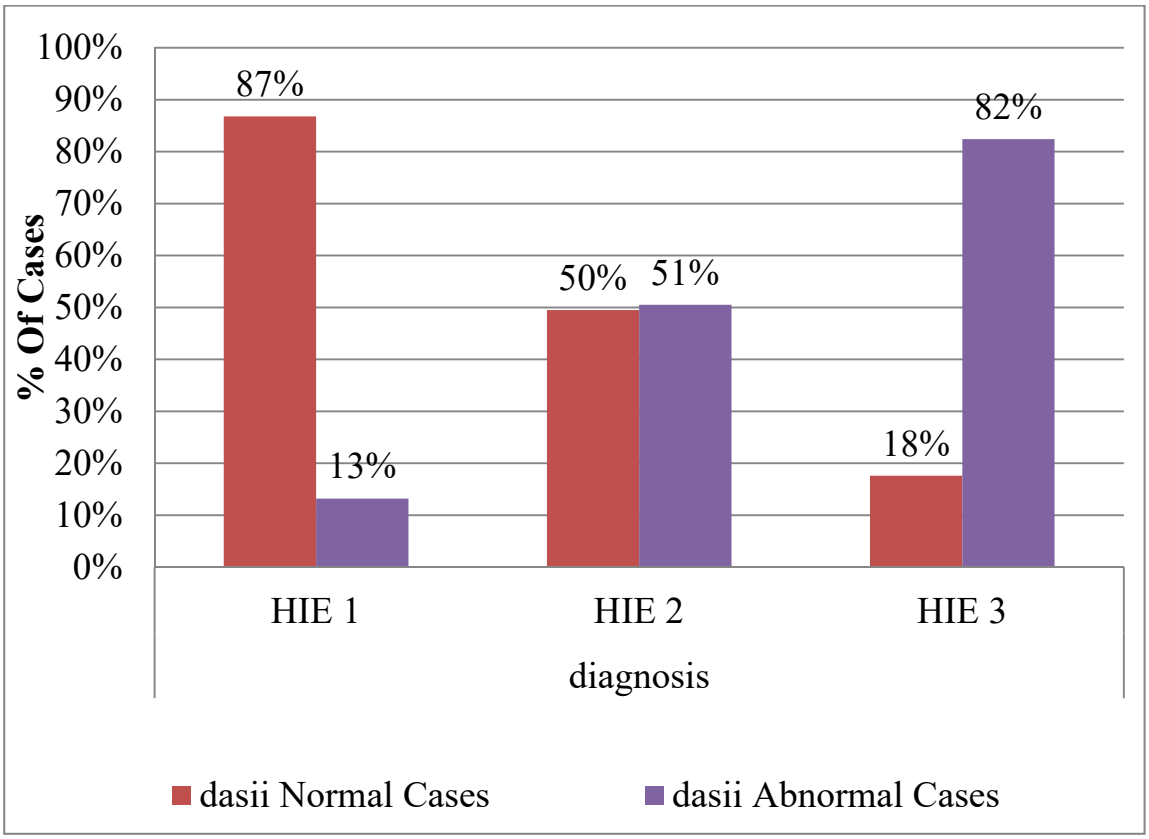


TABLE 21 - COMPARISION OF DEVELOPMENT OF HIE INFANTS AS PER DDST DURING FOLLOW UP AND DASII AT THE END OF FOLLOW UP.

Variable		DASII	
		Normal	Abnormal
DDST (3 month)	Normal	78	32
	Abnormal	3	37
DDST (6 month)	Normal	80	15
	Abnormal	1	54
DDST(9 month)	Normal	81	5
	Abnormal	0	64

TABLE 22- SENSITIVITY, SPECIFICITY, POSITIVE PREDICTIVE VALUE, NEGATIVE PREDICTIVE VALUE AND DIAGNOSTIC ACCURACY OF DDST

Parameter(DDST)	Sensitivity	Specificity	PP Value	NP Value	Diagnostic Accuracy
3rd month	96.3%	53.62%	70.91%	92.5%	76.67%
6th month	98.77%	78.26%	84.21%	98.18%	89.33%
9th month	100%	92.75%	94.19%	100%	96.67%

During 3rd month follow up, the sensitivity and specificity to identify developmental delay by DDST were 96.3% and 53.62%. Positive predictive value was 70.91% and negative predictive value was 92.5%.

Overall diagnostic accuracy was 76.67%.

During 6th month follow up, the sensitivity and specificity to identify developmental delay by DDST were 98.77% and 78.26%. Positive predictive value was 84.21 % and negative predictive value was 98.18 %.

Overall diagnostic accuracy was 89.33%.

During 9th month follow up, the sensitivity and specificity to identify developmental delay by DDST were 100% and 92.75%. Positive predictive value was 94.19 % and negative predictive value was 100 %.

Overall diagnostic accuracy was 96.67%.

TABLE 23- ASSOCIATION BETWEEN DEVELOPMENTAL DELAY AMONG THE HIE INFANTS AND NEONATAL REFLEX

Variable N (%)			DASII		p Value
			Normal	Abnormal	
NNR	normal	138 (92)	78 (96.2)	60 (86.9)	0.321
	abnormal	12 (8%)	3 (3.7)	9 (13)	

Among the 150 HIE cases, 138 cases (92 %) had normal neonatal reflex and 12 cases (8%) had abnormal neonatal reflex.

Among the 81 cases with normal developmental outcome by DASII, 78 cases(96.2%) had normal neonatal reflex and 3 cases (3.7%) had abnormal neonatal reflex.

Among the 69 cases with delayed developmental outcome by DASII, 60 cases (86.9%) had normal neonatal reflex and 9 cases(13%) had abnormal neonatal reflex.

A significant statistical difference (P value 0.321) was not found between neonatal reflex and developmental delay among HIE infants.

TABLE 24 - ASSOCIATION BETWEEN DEEP TENDON REFLEX AND DEVELOPMETAL DELAY AMONG HIE INFANTS

Variable N(%)			DASII		p Value
			Normal	Abnormal	
DTR	Normal	85 (56.6)	77 (95.1)	8 (11.6)	<0.001
	Abnormal	65 (43.3)	4 (4.9)	61(88.4)	

Among 81 cases wih normal developmental outcome, 77 cases (95.1%) had normal DTR and 4 cases (4.9%) had exaggerated DTR.

Among 69 cases wih delayed developmental outcome, 8 cases (11.6%) had normal DTR and 61 cases (88.4%) had exaggerated DTR.

A significant statistical association (P value 0.001) was found between abnormal deep tendon reflex and developmental delay among HIE nfants.

TABLE 25- ASSOCIATION BETWEEN DEVELOPMENTAL DELAY AMONG HIE INFANTS AND THEIR NEUROIMAGING

Variable N(%)			DASII		p Value
			Normal	Abnormal	
Neuroimaging	Normal	59 (39.3)	46 (56.8)	13 (18.8)	<0.001
	Mild Changes	62 (41.3)	34 (42)	28 (40.6)	
	Severe Changes	29 (19.3)	1 (1.2)	28 (40.6)	

Among the 150 HIE cases, 59 cases (39.3%) had normal neuroimaging, 62 cases (41.3%) had mild HIE changes, 29 cases (19.3%) had severe HIE changes in neuroimaging.

Among 81 HIE infants with normal developmental outcome, 46 cases (56.8%) had normal cranial imaging, 34 cases(42%) had mild changes in cranial imaging and 1 case (1.2%) had severe changes in cranial imaging.

Among 69 HIE infants with delayed developmental outcome, 13 cases (18.8%) had normal cranial imaging, 28 cases(40.6%) had mild changes in cranial imaging and 28 cases (40.6 %) had severe changes in cranial imaging.

A significant statistical association (P value 0.001) was found between developmental delay among HIE infants and cranial imaging.

DISCUSSION

DISCUSSION

Hypoxic ischemic encephalopathy (HIE) is known to be associated with significant morbidity and mortality in the full term infant.

This study was conducted to identify neurodevelopmental outcome of HIE infants and their outcome in relationship with the severity of HIE.

During the study period from march 2016 to October 2017, 150 HIE infants were followed. Among them more than half of the infants had HIE II and one third of the infants had HIE I and remaining were HIE III. The number of male infants were proportionately high in HIE I and HIE II and female infants are more in HIE III.

Infants with HIE, those delivered by primi mothers are more than multigravida mothers. HIE was more common in outborn babies than inborn babies.

Among the complications, shock and multiorgan dysfunction were more common in HIE III infants. Among the multiorgan dysfunction, we observed that acute kidney injury is most common [9].

We also observed that there was no significant statistical correlation with weight and length of the HIE infants and the severity of HIE. There was significant statistical association between severity of HIE and increase in number of days of NICU admission.

We found out a significant statistical association between tone abnormality and severity of HIE at first visit and 3rd , 6th, 9th , 12th month follow up visit.

There was a significant statistical correlation between the decrease in head circumference and severity of HIE during 6th, 9th, 12th month follow up visit. This correlates with Charlene et al [4] who stated that a decrease of head circumference growth in the early months, as determined by serial measurements, is associated with adverse outcome.

By DASII, some of HIE I infants, half of the HIE II infants, nearly all HIE III infants had developmental delay (DQ < 70). 15.8 % of HIE I infants, 49.5 % of HIE II and 94.1 % of HIE III had abnormal neurodevelopmental outcome[9] . In our study, percentage of abnormal neurodevelopmental outcome in HIE I infants were slightly high.

At 3rd month follow up, nearly all HIE I infants had normal DDST, one fourth of HIE II infants, two third of HIE III infants had abnormal DDST. It has sensitivity of 96.3 % and specificity of 53.6 % with overall diagnostic accuracy of 76.67% at 3rd month follow up.

At 6th month follow up, one seventh of HIE I infants, one third of HIE II infants, and all infants of HIE III had abnormal DDST. It has

sensitivity of 98.7 % and specificity of 78.2 % with overall diagnostic accuracy of 89.33% at 6th month follow up.

At 9th month follow up, one seventh of HIE I infants, one half of HIE II infants, and all infants of HIE III had abnormal DDST. It has sensitivity of 100% and specificity of 92 % with overall diagnostic accuracy of 96.67 % at 9th month follow up.

We observed significant statistical association between neuroimaging abnormality and severity of HIE. Thus, neuroimaging may helps to predict neurodevelopmental outcome in term infants with HIE. This finding was similar to the study done by Rebia et al[2] .

At first visit, 2 out of 38 HIE I infants, 6 out of 95 HIE II infants, 2 out of 17 HIE III infants had abnormal fundus findings. Some of them had bilateral temporal pallor, some had retinal hemorrage, few had retinopathy of prematurity also.

During follow up visit, there was decrease in abnormal fundus findings only 6 infants had abnormal fundus findings, remaining were found to be normal. Also we found out that some of infants who have normal fundus examination in previous visit developed convergent squint during follow up visit.

Also we observed no statistical significance between visual abnormality and severity of HIE.

By OAE screening test, 3 out of 38 HIE I infants, 20 out of 95 HIE II infants, 8 out of 17 HIE III infants had abnormal screening test. Those who have abnormal screening were undergone BERA and found out to be one abnormal.

RECOMMENDATIONS

RECOMMENDATIONS

From our study, we suggest follow up of all stages of HIE infants had significant role to detect developmental delay earlier. Hence they may be enrolled for early intervention to prevent severe sequelae.

Denver Developmental Screening Test (DDST) had been used in our study with reasonable sensitivity, specificity and diagnostic accuracy when compared with DASII (Developmental Assessment Scale For Indian Infants). Hence DDST can be used for follow up developmental assessment in office practice since it is less time consuming with good diagnostic accuracy.

Visual and hearing assessment is mandatory along with developmental assessment during follow up of HIE infants. Neuroimaging may help to predict the neurodevelopmental outcome of term infants with HIE.

Also head circumference and tone abnormality helps to predict developmental outcome on follow up.

LIMITATIONS

LIMITATIONS

Number of infants in HIE I and III were less when compared to HIE II infants in our cohort.

MRI brain could not be done in all cases.

ANNEXURES

BIBLIOGRAPHY

1. Caroline E A hearne et al, Short and long term prognosis in perinatal asphyxia: An *World J Clin Pediatr* 2016 February 8; 5(1):67-74 ISSN 2219-2808
2. Rabia G Sezer, Prediction of neurodevelopmental outcome in term Neonates with hypoxic-ischemic encephalopathy J Neonatal Biol 2016, 5:4, 9th International Conference on Neonatology and Pediatric Neurology November 28-30, 2016
3. Samantha et al, predicting neuro-developmental outcome with hypoxic ischemic encephalopathy by vojta's neurokinesiological examination
4. Department of Pediatrics, M.S. Ramaiah Medical College, Gokula Indian Pediatrics 1999;36:171-173
5. Perez et al, University of Zurich, Journal of Pediatrics, 163(2):454-459.e1.
6. Charlene et al., Follow-up of the term infant after hypoxic-ischemic Encephalopathy, Paediatr Child Health 2006;11(5):278-282.
7. Meena et al, IOSR Journal of Dental and Medical Sciences (IOSR-JDMS) e-ISSN: 2279-0853, p-ISSN: 2279-0861. Volume 13, Issue 3 Ver. I (Mar. 2014), PP 50-53.

8. Man xu et al, Int J Clin Exp Med 2016;9(3):6605-6612 Journal of Pediatric and Neonatal Individualized Medicine 2014;3(2):e030269
9. Ashaq H Thoker et al, American J Exp Clin Res 2017;4(2):206-209
10. Manual of neonatal care *I* editors, John P. Cloherty ... [et al.]. -7th ed.
11. Shellhaas RA, Soaita AI, Clancy RR. Sensitivity of amplitude-integrated electroencephalography for neonatal seizure detection. *Pediatrics* 2007;120(4):770-777.
12. Wirrell EC, Armstrong EA, Osman LD, et al. Prolonged seizures Exacerbate perinatal hypoxic-ischemic brain damage. *Pediatr &s* 2001;50(4):445-454.
13. McBride MC, I..aroia N, Guillet R Electrographic seizures in Neonates correlate with poor neurodevelopmental outcome. *Neurology* 2000;55(4):506-513.
14. Rennie J, Boylan G. Treatment of neonatal seizures. *Arch Dis Child Fetal Neonatal Ed* 2007;92(2):F148-F150
15. Gluckman PD, Wyatt JS, Azzopardi D, et al. Selective head cooling with mild systemic hypothermia after neonatal encephalopathy: multicentre randomised trial. *Lancet* 005;365 (9460) :663-670.
16. Shankaran S, Laptook AR, Ehrenkranz RA, et al. Whole-body Hypothermia for neonates with hypoxic-ischemic encephalopathy. *N Eng/]* Med2005;353(15):1574-1584.

17. Azzopardi DV, Strohm B, Edwards AD, et al. Moderate hypothermia To treat perinatal asphyxia encephalopathy. *N englm*ed2009;361(14):1349-1358.
18. Gunn AJ, Gluckman PD, Gunn TR Selective head cooling in newborn infants after perinatal asphyxia: a safety study. *Pediatrics* 1998;102 (4 pt 1):885-892.
19. Eicher DJ, Wagner CL, Katikaneni LP, et al. Moderate hypothermia in neonatal encephalopathy: safety outcomes. *Pediatr* Neurol2005;32(1): 18-24.
20. Shankaran S, Pappas A, Laptook AR, et al. Outcomes of safety and effectiveness in a multicenter randomized, controlled trial of whole-body hypothermia for neonatal hypoxic-ischemic encephalopathy. *Pediatrics* 2008; 122(4) :e791-e798.
21. Edwards AD, Brocklehurst P, Gunn AJ, et al. Neurological outcomes at months of age after moderate hypothermia for perinatal hypoxic, ischemic encephalopathy: synthesis and meta-analysis of trial data. BM]2010;340:c363. Groenendaal F, De Vooght KM, van Bel E Blood gas values during Hypothermia in asphyxiated term neonates. *Pediatrics* 2009; 123(1): 170-172.
22. Holmes G, Rowe J, Hafford J, et al. Prognostic value of the Electroencephalogram in neonatal asphyxia. *Electroencephalogr Clin Neurophysiol1982;53(1):60-72.*

23. Johnston MY, Trescher WH, Ishida A, et al. Neurobiology of hypoxic-ischemic injury in the developing brain. *Pediatr Res* 2001;49(6):735-741.

24. Barkovich AJ, Westmark K, Partridge C, et al. Perinatal asphyxia: MR findings in the first 10 days. *A]NRAm] Neuroradiol1995;16(3): 427--438.*

25. Meberg A, Broch H. Etiology of cerebral palsy.] *Perinat m*ed2004 ;32(5):434--439.

26. Sarnat HB, Sarnat MS. Neonatal encephalopathy following fetal distress. A clinical and electroencephalographic study. *Arch* Neuroli 976;33(10):696—705.

27. Soul JS, Robertson RL, Tzika AA, et al. Time course of changes in diffusion-weighted magnetic resonance imaging in a case of neonatal encephalopathy with defined onset and duration of hypoxic-ischemic insult. *Pediatrics* 200 I; I 08 (5): 12II-I2I4.

28. Volpe JJ. *Neurology of the Newborn.* 5th ed. Philaddphia, PA: Saunders Elsevier; 2008.

29. Illingworth RS. The Development of the Infant and Young child: Normal and Abnormal, 9th edition. Haryana: Reed Elsevier Private Limited; 2010 Malhi P. Screening young children for delayed development. Indian Pediatr.1999;36:569-77.

30. Nair MKC, Babu G, Sabarinathan. CDC grading for head holding sitting and standing. Indian J Pract Pediatr. 1995;3(1):53-4.
31. Nair MKC, George B. Trivandrum Developmental Screening Chart (TDSC). Indian Pediatr. 1991;28:869-72.
32. Nair MKC, Jain N, Murkhi S, et al. The High Risk Newborn. New Delhi: Jaypee Brothers Medical Publishers (P) Ltd; 2007.
33. Nair MKC. Early stimulation CDC Trivandrum model. Indian J Pediatr. 1992;59:663-7.
34. Nair MKC. Editorial: simplified developmental assessment. Indian Pediatr. 1991;28:837-40.
35. Indian Pediatrics. (2009). Supplement Issue on Child Development. [Online] Indian Pediatrics website. Available from http://www.indianpediatrics.net/suppl2009/supple.

PROFORMA

Name : DOB :

Age/ sex : B.wt :

Address : Inborn/Outborn

Contact no:

AN H/O : G P L A

H/O GDM /PIH /Maternal fever /APH

AN scan abnormality -

Birth H/O : gestational age -

NVD/AVD/Emergency LSCS/elective LSCS

B.wt - SGA/AGA/LGA

Resuscitation - no need /need /apgar

PN H/O : N ICU admission (no of days) :

NNC : +/_ duration of AEDs :

Ventilation : not required / uncomplicated course/> 7 days

Shock : no / yes / refractory

Hypoglycaemia : transient /<25 mg for > 3 days/symptomatic

multiorgan injury : +/_

sepsis : suspected / sepsis / meningitis

NNJ : phototherapy/exchange transfusion/ kernicterus

DBF on - th day ABX - days

DIAGNOSIS -

At discharge : neurological examination NORMAL / severe prolonged encephalopathy / abnormal with suspect developmental delay

Home environment: good / suboptimal

Examination

Length :

Weight :

HC :

Tone : hypo / hyper symmetric/asymmetric

NNR : +/-

DTR : +/-

Vision :

Hearing :

INVESTIGATIONS

CT brain/ NSG / MRI brain :

Vision :

Hearing :

Others :

FOLLOW UP

Overall assessmentof neuromotor and developmental status (3,6,9,12,15 months)

date	**CA**	**tone**	**Develop mental age**	**HC**	**Seizures +/_**	**Involuntary movements +/-**	**vision**	**hearing**	**others**	**Normal/ Suspect/ abnormal**

Muscle tone assessment (amiel tison)

Age(mon)	**date**	**Adductor angle**		**Popliteal angle**		**Dorsiflexion angle**		**Scarf sign**
0-3		40-80		80-100		60-70		Elbow not cross midline
4-6		70-120		90-120		”		Crosses midline
7-9		110-140		110-160		”		Goes beyond axillary line
10-12		140-160		150-170		”		

MASTER CHART

name	sex	GPLA	antenatal risk	O/I	mode of delivery	resuscitation	NICU admission	NNC	Ventilation	shock	hypoglycemia	multi organ injury	sepsis	diagnosis	length	wt
baby.nithin	m	1	1	O	1	2	13	+	-	-	-	-	-	HIE 2	46	2.6
b/o nithya	m	1	-	o	1	2	14	+	+	-	-	AKI	-	HIE 3	48	3.2
b/o kanimzhi	m	2	2	I	3	-	7	+	-	-	-	-	-	HIE 2	47	4
b/o geetha	m	1	-	o	1	3	20	-	+	+	-	+	+	HIE 3	45	2.7
b/o riswanabarwin	m	1	1	I	1	2	7	-	-	-	-	-	+	HIE 1	46	2.9
b/o veerammal	m	2	-	o	1	2	10	+	-	-	-	-	-	HIE 2	45	3
b/o laxmi	m	1	3	I	1	1	5	-	-	-	-	-	-	HIE 1	45.2	2.8
b/o chingapandi	m	1	-	O	1	2	15	+	-	-	-	-	-	HIE2	48	2.8
b/o vasuki	m	2	1	I	1	2	7	+	-	-	-	-	-	HIE2	52	3.5
b/o rajalaxmi	m	1	3	I	1	2	10	-	-	-	-	-	+	HIE1	52	4
b/o kaviyasri	f	2	-	I	1	1	10	+	-	-	-	-	-	HIE2	48	2.5
b/o sathya	f	2	-	I	1	3	15	+	+	+	-	-	+	HIE2	46.8	2.5
b/o solaiammal	f	1	-	O	1	1	15	+	-	-	-	-	+	HIE2	47	3
baby venkateshwari	f	2	1	O	1	2	14	+	-	-	-	-	+	HIE2	48.5	3.5
b/o kokila	f	2	-	O	2	2	20	+	+	+	-	+	+	HIE3	44.5	3.2
b/o verammal	m	1	-	I	1	1	14	+	-	-	-	-	+	HIE2	52	2.7
b/o janaki	m	1	-	O	1	2	18	+	-	-	-	-	-	HIE2	52	3.5
b/o umesh	m	1	1	I	3	2	6	-	-	-	-	-	-	HIE1	51	2.8
b/o devi	f	2	-	I	1	1	1	+	-	-	-	-	-	HIE2	50	2.6
b/o kavitha	m	2	-	O	2	2	17	+	+	+	-	AKI+	+	HIE3	49	2.5
b/o nishanti	m	2	-	O	1	2	7	+	-	-	-	-	-	HIE2	48.5	2.6
b/o rajeshwari	f	1	-	O	1	2	20	-	+	+	-	-	+	HIE3	47.8	2.4
b/o sumathy	f	1	-	O	1	1	7	+	-	-	-	-	-	HIE2	46.5	2.3
baby veeramanikandan	m	1	1	O	1	2	12	+	-	-	-	-	-	HIE2	48	2.5
b/o pandeshwari	m	1	-	O	1	2	13	+	-	-	-	-	-	HIE2	49	2.8
siddharth	m	1	1	O	1	2	14	+	-	-	-	-	+	HIE2/sepasis	48.2	2.1
krithick	m	1	1	O	1	2	9	+	CPAP2d	-	-	-	+	hie2/msa	46	3.7
sabirashree	f	1	2	I	3	3	7	-	CPAP 1d	-	-	-	-	HIE1	50	3.2
sanjanashree	f	1	-	I	1	1	8	+	-	-	-	-	-	HIE2	51	3.2
b/o karuppayya	m	2	1	I	4	2	25	+	CPAP 1d	-	-	-	+	HIE2	52	2.8
b/o asaikili	m	1	-	I	1	2	6	+	-	-	-	-	-	HIE2	52.1	3.2
b/o nandhini	m	1	1	I	2	3	13	-	-	-	-	-	-	HIE1	47	3
madhara	m	1	-	O	1	2	15	+	CPAP 1d	-	-	-	+	HIE2	48.2	3
b/o vanitha	m	2	2	O	1	2	5	-	-	-	-	-	-	HIE1	49.6	2.5
b/o vijayalaxmi	m	2	-	I	1	2	4	+	-	-	-	-	-	HIE2	45.2	3.5
nadashree	f	1	-	I	3	2	17	+	-	-	-		+	HIE2	46.5	2.5

b/o meenakshi	m	1	-	I	1	2	9	+	CPAP 1d	-	-	-	+	HIE2	47	2.5
veeramanikandan	m	2	1	O	1	2	8	+	-	-	-	-	-	HIE2	48	3.5
b/o bhuvaneshwari	m	1	2	I	3	-	3	-	-	-	-	-	-	HIE1	47	1.75
sivarithishri	f	1	1	I	1	2	9	+	-	-	-	-	+	HIE2	48	4.3
dhivnesh	m	1	-	I	3	2	7	+	CPAP 2D	-	-	-	+	HIE2	47	2.75
jeeva	m	1	1	I	3	2	7	-	-	-	-	-	-	HIE1	50	3.5
b/o sundaradevi	m	1	2	I	1	2	7	-	-	-	-	-	-	HIE1	50	3.5
aniruth	m	1	3	I	3	2	15	-	-	-	-	-	+	HIE1	50.2	3.2
b/o indira	f	1	-	I	1	2	15	+	-	-	-	-	-	HIE2	51	3
b/o gee tha	m	1	1	O	1	2	13	+	-	-	-	-	-	HIE2	46	2.6
b/o vanitha	f	1	-	O	1	2	14	+	+	+	-	+	-	HIE3	48	3.2
b/o vijaya	m	2	-	I	3	-	7	+	-	-	-	-	-	HIE2	47	4
b/o boomani	m	1	-	O	1	3	20	+	+	+	-	-	+	HIE3	45	2.7
b/o shanmugasundari	m	1	1	I	1	2	7	-	-	-	-	-	+	HIE1	46	2.9
b/o anusha	m	2	-	O	1	2	10	+	-	-	-	-	-	HIE2	45	3
b/o veni	f	1	2	I	1	1	5	-	-	-	-	-	-	HIE1	47	2.8
b/o saraswathi	m	1	-	O	1	2	15	+	-	-	-	-	-	HIE2	48	2.8
b/o devi	f	2	-	I	1	2	7	+	-	-	-	-	-	HIE2	52	3.5
b/o poornima	f	1	1	I	1	2	10	-	-	-	-	-	+	HIE1	52	4
b/o prakashi	f	2	-	I	1	1	10	+	+	-	-	-	-	HIE2	50	3.5
b/o selvi	f	2	-	I	1	3	15	+	+	+	-	AkI	+	HIE3	51	2.5
b/o seetha	f	2	-	O	1	1	15	+	-	-	-	-	+	HIE2	51.2	2.8
b/o madhu	f	1	-	O	1	2	14	+	-	-	-	-	+	HIE2	50.3	2.9
b/o amaravathi	f	2	-	O	1	2	20	+	+	+	-	+	+	HIE3	52	2.9
b/o kani	f	2	1	I	1	1	14	+	-	-	-	-	+	HIE2	52	2.7
b/o murkeshwari	m	1	-	O	1	2	18	+	-	-	-	-	-	HIE2	52	3.5
b/o parvathasri	m	1	1	I	3	2	6	+	-	-	-	-	-	HIE2	51	2.8
b/o majula	f	2	-	I	1	1	7	-	-	-	-	-	-	HIE1	50	3.5
b/o sorna	m	2	-	O	2	2	17	+	+	-	-	-	-	HIE2	50	3.4
b/o devi	m	2	1	O	1	2	7	+	-	-	-	-	+	HIE2	50	3.9
b/o nayaki	f	1	-	O	1	2	20	+	+	+	-	-	-	HIE3	49	2.8
b/o baby	f	1	-	O	1	1	7	+	+	-	-	-	+	HIE2	55	4.1
b/o sutha	m	1	-	O	1	2	12	+	-	-	-	-	-	HIE2	49.5	2.9
b/o parvathi	m	1	-	O	1	2	13	+	-	-	-	-	-	HIE2	49	2.7
b/o afrin	m	1	-	O	1	2	14	+	-	-	-	-	-	HIE2	48	2.1
b/o aarthi	m	1	1	O	1	2	9	+	+	-	-	-	+	HIE2	48.2	3.7
b/o anandhi	f	1	-	I	3	3	7	+	+	-	-	-	+	HIE2	48.7	3.2
b/o sachu	f	1	1	I	1	1	8	-	-	-	-	-	-	HIE1	47	3.2
b/o uma	m	2	1	I	4	2	25	+	+	-	-	-	-	HIE2	45	2.8
b/o mangai	m	1	1	I	1	2	6	+	-	-	-	-	+	HIE2	46	3.2
b/o bavani	m	1	-	I	2	3	13	+	-	-	-	-	-	HIE2	46.7	3

b/o gowri	m	1	1	O	1	2	15	-	-	-	-	-	-	HIE1	45.5	3
b/o vasanthi	m	2	-	O	1	2	5	+	-	-	-	-	+	HIE2	48	2.5
b/o kavitha	m	2	-	I	1	2	4	-	-	-	-	-	-	HIE1	48	3.5
b/o subha	f	1	-	I	3	2	17	+	-	-	-	-	-	HIE2	49	2.5
b/o chithra	m	1	-	I	1	2	9	+	+	-	-	-	+	HIE2	49.2	2.5
b/o selvi	m	2	-	O	1	2	8	+	-	-	-	+	+	HIE2	50	3.5
b/o soniya	m	1	-	I	3	-	3	+	-	-	-	-	-	HIE2	50.6	1.75
b/o sneha	f	1	-	I	1	2	9	-	-	-	-	-	-	HIE1	50.8	4.3
b/o chandra	m	1	-	I	3	2	7	-	-	-	-	-	+	HIE1	50	2.75
b/o divya	m	1	1	I	3	2	7	+	-	-	-	-	+	HIE2	49	2.75
b/o kumari	m	1	-	I	1	2	7	+	-	-	-	-	-	HIE2	48	3.5
b/o sangari	m	1	-	I	3	2	15	-	-	-	-	-	-	HIE1	48	2.5
b/o muhila	m	1	1	O	1	2	13	-	-	-	-	-	+	HIE1	46	3
b/o viji	f	1	-	O	1	2	14	-	-	-	-	-	-	HIE1	48	3.2
b/o lalitha	m	2	-	I	3	-	7	+	-	-	-	-	-	HIE2	47	4
b/o malathi	m	1	-	O	1	3	20	+	+	+	-	+	-	HIE3	45	2.7
b/o padhma	m	1	1	I	1	2	7	+	-	-	-	-	+	HIE2	46	2.9
b/o bharathi	m	2	-	O	1	2	10	+	-	-	-	+	+	HIE3	48	3
b/o sri devi	f	1	-	I	1	1	5	-	-	-	-	-	-	HIE1	49	2.8
b/o mumtaj	m	1	-	O	1	2	15	+	-	-	-	-	-	HIE2	49	2.8
b/o amutha	f	2	-	I	1	2	7	-	-	-	-	-	-	HIE1	52	3.5
b/o rani	f	1	1	I	1	2	10	+	-	-	-	-	-	HIE2	52	4
b/o viji	m	2	-	o	1	2	4	-	-	-	-	-	-	HIE1	51	2.5
b/o ananthi	M	1	-	I	1	1	14	+	-	-	-	-	+	HIE2	52	2.7
b/o selvarani	M	1	-	O	1	2	18	+	-	-	-	-	-	HIE2	52	3.5
b/o maheshwari	M	1	1	I	3	2	6	-	-	-	-	-	-	HIE1	52	2.8
b/o Thivya	F	2	-	I	1	1	7	+	-	-	-	-	-	HIE2	50	2.5
b/o pushpam	M	1	-	O	2	2	17	+	+	-	-	AKI+	+	HIE2	52	2.8
b/o nishanti	M	2	-	O	1	2	7	+	-	-	-	-	-	HIE2	51	2.9
b/o nirmala	F	1	-	O	1	2	20	-	+	+	-	-	+	HIE3	52	3
b/o malathy	F	1	-	O	1	1	7	+	-	-	-	-	-	HIE2	55	4.1
b/o gowsi	M	1	1	O	1	2	12	+	-	-	-	-	-	HIE2	46	2.6
b/o bagavathy	m	1	1	O	1	2	13	+	-	-	-	-	-	HIE2	48	3.2
b/o indhu mathi	f	1	-	O	1	2	14	+	+	+	-	-	-	HIE3	47	4
b/o iswariya	m	2	-	I	3	-	7	+	-	-	-	-	-	HIE2	45	2.7
b/o hema	m	1	3	O	1	3	20	-	+	+	-	+	+	HIE3	46	2.9
b/o jisha	m	1	1	I	1	2	1	-	-	-	-	-	+	HIE1	42.5	3
b/o preethi	m	2	-	O	1	2	10	+	-	-	-	-	-	HIE2	47	2.8
b/o nachiyar	f	1	-	I	1	1	5	-	-	-	-	-	-	HIE1	48	2.8

b/o varsha	m	1	-	O	1	2	15	+	-	-	-	-	-	HIE2	48	3.5
b/o afrin	f	2	-	I	1	2	7	+	-	-	-	-	-	HIE2	52	4
b/o banu	f	1	1	I	1	2	10	-	-	-	-	-	CRP+	HIE1	52	3.5
b/o selva kumari	f	2	-	I	1	1	10	+	-	-	-	-	-	HIE2	52	2.5
b/o brintha	f	2	2	I	1	3	15	+	+	+	-	+	+	HIE3	50	2.5
b/o harini	f	1	-	O	1	1	15	+	-	-	-	-	+	HIE2	51	2.9
b/o saroja	f	2	-	O	1	2	14	+	-	-	-	-	+	HIE2	51	2.8
b/o anubraba	f	2	1	O	2	2	20	+	+	+	-	+	+	HIE3	44.5	2.7
b/o nanthini	m	1	2	I	1	1	14	+	-	-	-	-	+	HIE2	52	2.7
b/o esakkiammal	m	1	2	O	1	2	18	+	-	-	-	-	-	HIE2	52	3.5
b/o pavithra	m	1	1	I	3	2	6	+	-	-	-	-	-	HIE2	52	2.8
b/o karthika	f	2	-	I	1	1	1	-	-	-	-	-	-	HIE1	48	2.6
b/o lavaniya	m	2	-	O	2	2	17	+	+	-	-	AKI+	+	HIE2	49	2.5
b/o bavani	m	1	-	O	1	2	13	+	-	-	-	-	-	HIE2	48	2.8
b/o jayanthi	m	1	1	O	1	2	14	+	-	-	-	-	+	HIE2	48	2.1
b/o kalyani	m	1	1	O	1	2	9	+	CPAP 2d	-	-	-	+	HIE2	49	3.7
b/o pappu	f	1	1	I	3	3	7	-	CPAP1d	-	-	-	-	HIE1	47	3.2
b/o avudaiammal	f	1	2	I	1	1	8	+	-	-	-	-	-	HIE2	47	3
b/o seyad ali fathima	m	2	1	I	4	2	25	+	CPAP 1d	-	-	-	+	HIE2	47	2.8
b/o mary grace	m	1	-	I	1	2	6	+	-	-	-	-	-	HIE2	47.8	3.2
b/o joy rani	m	1	-	I	2	3	13	-	-	-	-	-	-	HIE1	47.9	3
b/o nagash wari	m	1	-	O	1	2	15	+	CPAP1d	-	-	-	+	HIE2	48	3
b/o bakiyam	m	2	-	O	1	2	5	-	-	-	-	-	-	HIE1	45	2.5
b/o sumithra	m	2	-	I	1	2	4	+	-	-	-	-	-	HIE2	48	3.5
b/o renuka	f	1	-	I	3	2	17	+	-	-	-	-	+	HIE2	49	2.5
b/o rukmani	m	1	3	I	1	2	9	+	CPAP1d	-	-	-	+	HIE2	50	2.5
b/o banumathi	m	2	1	O	1	2	8	+	-	-	-	-	-	HIE2	51	3.5
b/o soranam	m	1	3	I	3	-	3	-	-	-	-	-	-	HIE2	52	1.75
b/o letricia	f	1	1	I	1	2	9	-	-	-	-	-	+	HIE1	51	4.3
b/o piramachi	m	1	-	I	3	2	7	+	CPAP1d	-	-	-	+	HIE2	52	2.75
b/o leema	m	1	1	I	3	2	7	+	-	-	-	-	-	HIE2	50	2.3
b/o logamal	m	1	-	I	1	2	7	-	-	-	-	-	-	HIE1	52	3.5
b/o priya sundari	m	1	-	I	3	2	15	-	-	-	-	-	+	HIE1	50	2.5
b/o deepa	f	2	-	o	3	1	5	-	-	-	-	-	-	HIE1	46	3

hc	tone	NNR	DTR	neuroimaging	vision	hearing	hc1	tone1	ddst1	hc2	tone2	ddst2	hc3	tone3	Vision 2	hearing2	ddst3	hc4	tone4	dasii
34.6	N	+	+	2	N	1	37	N	N	39	N	N	40	N	N	N	N	41	N	N
34	1	+	++	3	1	2	37	1	N	40	2	S	42	2	N	N	DD	44	2	3
37	N	+	+	2	N	1	39	N	N	40	N	N	41	N	N	N	N	41.5	N	N
36.5	1	+	++	3	N	1	38	1	S	39	2	DD	41	2	N	N	DD	43	2	3
36	N	+	+	1	N	1	38	N	N	40	N	N	41	N	N	N	N	42	N	N
36	1	-	-	3	1	1	36	1	S	37	2	DD	38	2	N	N	DD	38.5	N	3
36.2	N	-	+	1	N	1	35	N	N	37	N	N	40	N	N	N	N	42	N	N
35	N	+	+	2	2	1	39	N	N	42	N	N	42	N	N	N	S	43	N	1
36	N	+	+	1	N	1	39	N	N	41.5	N	N	43	N	N	N	N	45	N	N
36	N	+	+	1	N	1	38	N	N	40	N	N	43	N	N	N	N	45	N	N
34.7	N	+	+	2	2	1	37	N	N	39.5	N	N	42	N	N	N	N	44	N	N
33	1	+	-	3	N	2	33.2	2	DD	33.5	2	DD +	34	2	N	N	DD	34	2	5
34	N	+	+	2	N	2	37	N	N	39.5	N	N	41.3	N	N	N	N	43	N	N
33	N	+	-	2	N	1	35	N	N	37.5	2	DD +	38	2	squint +	N	DD	40	2	3
36	2	+	++	3	1	2	36	2	S	35.8	2	DD +	36.5	2	N	N	DD	37	2	4
36	N	+	+	2	N	1	38	N	N	41	N	N	43	N	N	N	N	45	N	1
35.5	1	+	-	3	1	1	36	1	DD	36	1	DD +	36.8	1	N	N	DD	38	1	4
33	N	+	+	1	N	1	37	N	N	41	N	N	43	N	N	N	N	45	N	N
33	N	+	+	2	N	1	35	N	N	39	N	N	42	N	N	N	N	44	N	N
35.8	1	-	-	3	1	2	37	1	S	39	2	DD	41	2	N	ABNORMAL	DD	45	2	3
34	1	+	+	2	N	1	38.5	N	N	41	N	N	42.5	N	N	N	N	44	N	N
35	2	+	++	3	N	1	36	2	S	36.5	2	DD	37	2	N	N	DD	37	2	3
34.5	N	+	-	2	N	1	37	N	N	39	N	N	42	N	N	N	S	44	N	1
33	N	+	+	2	N	1	36	N	N	39	N	N	42	N	N	N	N	45	N	N
33	N	+	-	2	N	1	37	N	DD	40	N	DD	43	N	N	N	DD	45	N	4
35	1	-	-	3	2	1	37	2	DD	37.5	2	DD	38	2	N	N	DD	39	2	5
34	N	+	+	2	N	1	35	N	N	37	N	N	40	N	N	N	N	43	N	N
37	N	+	+	1	N	1	41.5	N	N	43	N	N	44	N	N	N	N	45	N	N
35	1	-	-	3	N	1	37	1	DD	38.5	1	DD	39	1	N	N	DD	39.2	1	4
37	N	+	+	2	N	1	39	N	N	42	N	N	43	N	N	N	N	44.2	N	N
33	N	+	+	2	N	1	36.5	N	N	39.5	N	N	41	N	N	N	N	43	N	N
35	N	+	-	1	N	1	37	N	N	39	N	DD	40.5	N	N	N	DD	42	N	3
34	N	+	+	2	N	1	39	N	N	41.5	N	N	43	N	N	N	N	45	N	N
34	N	+	+	1	N	1	36	N	N	38	N	N	41.5	N	N	N	N	43	N	N
34	N	+	+	2	N	1	37	N	N	39.5	N	S	40.5	N	N	N	S	43	N	2
32	N	+	+	3	N	1	33	N	N	34	N	N	36	N	squint +	N	N	38	N	N

35	N	+	+	2	N	1	39.7	N	N	42	N	N	43.5	N	N	N	N	45	N	N
38	N	+	-	2	N	2	39.5	N	N	42	N	N	46	N	N	N	S	47	N	2
35	N	+	-	1	N	1	38	N	N	41	N	S	41.5	N	N	N	DD	42.5	N	3
35	N	+	+	2	N	1	38	N	N	42	N	N	44	N	N	N	N	45	N	N
35.2	N	+	+	2	N	1	37	N	N	42.5	N	N	44	N	N	N	N	45.2	N	N
33	N	+	+	1	N	1	37	N	N	40	N	N	42.5	N	N	N	N	43.5	N	N
35.5	N	+	+	1	N	1	39.5	N	N	41.5	N	N	43	N	N	N	N	45	N	N
34	N	+	+	1	N	1	39.8	N	N	41	N	N	42	N	N	N	N	43.6	N	N
33	N	+	+	1	N	1	37	N	N	40	N	N	42.7	N	N	N	N	44	N	N
34.6	N	+	+	2	N	1	37	N	N	39.9	N	N	41.5	N	N	N	N	43	N	N
32.5	N	+	++	3	1	1	35	N	N	38	N	S	40	N	N	N	DD	42	N	3
37	N	+	+	2	N	2	38	N	N	40	N	N	41.5	N	N	N	N	43	N	N
36.5	1	+	-	3	N	1	38	1	S	39	2	DD	41	2	N	N	DD	41.2	2	3
36	N	+	+	1	N	2	40	N	N	42	N	N	43	N	N	N	N	44.2	N	N
36	1	+	-	3	1	1	39.8	1	S	41	2	DD	41.7	2	N	N	DD	43	2	3
36.2	N	+	+	1	N	1	40.5	N	N	42.7	N	N	44	N	N	N	N	45	N	N
35	N	+	-	2	2	2	39	N	N	42	N	N	43.5	N	N	N	S	45	N	1
34	N	+	+	2	N	1	39.7	N	N	42	N	N	43.5	N	N	N	N	44.8	N	N
36	N	+	+	1	N	1	39	N	N	41.2	N	N	43	N	N	N	N	44.7	N	N
34.7	N	+	+	2	2	1	37.8	N	N	39.5	N	N	41.5	N	N	N	N	43	N	N
33	1	+	-	3	N	2	33.2	2	DD+	33.5	2	DD+	34	2	N	N	DD	34	2	5
33	N	+	+	1	N	2	37	N	N	39.5	N	N	41	N	N	N	N	42.8	N	N
33	N	+	-	2	N	1	38	N	N	37.5	2	DD+	39	2	squint +	N	DD	40	2	3
36	2	+	-	3	2	2	38	2	S	40.5	2	DD+	42	2	N	N	DD	43.7	2	4
36	N	+	+	2	N	1	36.2	N	N	39	N	S	41	N	N	N	S	43	N	1
35.5	1	+	-	3	1	1	36	1	DD	37	1	DD+	37.8	1	N	N	DD	38	1	4
34	N	+	+	1	N	1	40	N	N	43	N	N	44	N	N	N	N	45	N	N
35	N	+	+	2	N	1	40	N	N	42.5	N	N	44	N	N	N	N	45.8	N	N
33	N	+	++	1	1	2	39	N	S	41	N	DD	42.7	N	N	N	DD	43	N	2
33.5	1	-	-	2	N	1	38	N	N	41	N	N	42.8	N	N	N	N	44	N	N
34.5	2	+	++	3	N	1	39.5	2	S	40.2	2	DD	42	2	N	N	DD	42.7	2	3
33	N	+	+	2	N	1	37.5	N	N	39.8	N	N	41.8	N	N	N	N	43	N	N
34	N	+	-	2	N	1	39.8	N	N	41.5	N	DD	43	N	N	N	DD	45	N	3
34.2	N	+	-	1	N	1	37	N	N	41	N	N	42.8	N	N	N	N	44	N	1
35	1	-	-	3	2	1	40	2	DD	41	2	DD	41.2	2	N	N	DD	43.6	2	4
34	N	+	++	2	N	1	38	N	DD	41	N	DD	42	N	N	N	DD	42.3	N	4
33.5	N	+	-	1	N	1	38	N	N	40	N	N	41.8	N	N	N	S	44	N	1
35	1	-	++	2	N	1	36.5	1	N	37	1	S	38	1	N	N	DD	38.2	1	3
37	N	+	++	2	2		39	N	DD	40.7	N	DD	42	N	N	N	DD	43.8	N	4
36	N	+	+	2	N	1	39.5	N	N	42	N	N	43.5	N	N	N	S	45	N	1
35	N	+	+	2	1	1	38	N	N	41	N	N	42.5	N	N	N	N	44	N	N

35	N	+	+	1	N	1	38	N	N	40.8	N	N	42	N	N	N	N	44.2	N	N
33.6	N	+	-	2	N		38	N	DD	41	N	DD	43	N	N	N	DD	45	N	3
34	N	+	+	1	N	1	39	N	N	41.3	N	N	43	N	N	N	N	44.7	N	N
32	N	+	+	2	N	1	33.5	N	N	34	N	N	36	N	squint +	N	N	38	N	N
35	N	+	+	2	N	1	39	N	N	42.8	N	S	43	N	N	N	S	44.8	N	2
35	N	+	+	1	N	2	38	N	N	42	N	N	43.6	N	N	N	N	45	N	N
35	N	+	-	2	N	1	39	N	N	41.6	N	S	43	N	N	N	DD	45	N	2
33	N	+	-	1	N	1	38	N	N	42	N	N	44	N	N	N	S	45.2	N	2
32	N	+	+	2	N	1	37	N	N	42.5	N	N	43.5	N	N	N	N	44.8	N	N
34.2	N	+	+	1	N	1	39	N	N	42	N	N	42.8	N	N	N	N	43.5	N	N
35.5	N	+	+	1	N	2	41	N	N	42.8	N	N	43	N	N	N	N	44.2	N	N
35	N	+	+	1	N	1	40	N	N	41	N	N	42	N	N	N	N	44	N	N
34.6	N	+	+	2	N	1	40	N	N	43	N	N	43.8	N	N	N	N	45	N	N
32.5	N	+	+	2	1	1	41	N	N	42.5	N	N	44	N	N	N	N	45.2	N	N
37	N	+	-	2	N	1	38	N	S	41	N	S	43	N	N	N	S	44.2	N	1
36.5	1	+	-	3	N	1	40	1	N	39	1	DD	41	N	N	N	DD	43	N	4
36	N	+	+	2	N	1	39	1	S	41.8	N	N	43	N	N	N	N	45	N	N
36	1	-	-	3	1	2	39.8	N	DD	41	2	DD	41.5	2	N	N	DD	43	3	5
36.2	N	+	-	1	N	1	39	N	DD	41.8	N	DD	43	N	N	N	DD	44.2	N	3
35	N	+	+	2	2	2	41	N	N	42	N	N	43.5	N	N	N	N	45	N	N
36	N	+	-	1	N	1	40	N	N	42.7	N	N	44	N	N	N	S	45	N	1
36	N	+	+	1	N	1	41.5	N	N	43.5	N	N	45	N	N	N	N	46	N	N
35	N	+	+	2	3	1	38	N	N	41	N	N	43	N	N	N	N	45	N	N
36	N	+	+	2	N	1	36.2	N	N	39	N	S	41	N	N	N	S	43	N	1
35.5	1	+	-	3	1	1	36	2	DD	37.5	1	DD+	39	1	N	N	DD	39.2	1	4
33	N	+	+	1	N	1	38	N	N	43	N	N	44	N	N	N	N	45.2	N	N
33.3	N	+	+	2	N	2	38.5	N	N	40	N	N	42	N	N	N	N	44	N	N
34.3	N	+	++	1	1	2	39	N	S	42	N	DD	43.5	N	N	N	DD	45	N	2
34.5	1	-	-	2	N	1	38.5	N	N	41	N	N	43	N	N	N	N	44.8	N	N
33	2	+	-	3	N	1	38	1	S	38.5	2	DD	39	2	N	N	DD	40	2	3
37.5	N	+	-	2	N	1	41	N	N	43.5	N	N	44	N	N	N	N	45	N	1
33.6	N	+	+	1	N	1	39	N	N	41.7	N	N	42.5	N	N	N	N	44	N	N
34.6	N	+	+	2	N	1	38	N	N	39.8	N	N	41.5	N	N	N	N	43	N	N
32.5	N	+	-	2	1	2	38	N	N	39	N	S	42.5	N	N	N	DD	44	N	1
37	N	+	+	2	N	2	38	N	N	41.2	N	N	43	N	N	N	N	45	N	N
36.5	1	+	-	3	N	1	38	1	S	39	1	DD	41	1	N	N	DD	41.7	1	3
36	N	+	+	1	N	1	40	N	S	42.7	N	N	43	N	N	N	N	45	N	N
36	1	+	-	3	1	1	38	1	DD	41	2	DD	41.8	2	N	N	DD	43	2	3
36.2	N	+	+	1	N	1	40	N	N	43	N	N	44	N	N	N	N	45	N	N

35	N	+	+	2	2	1	39	N	N	42	N	N	43	N	N	N	N	44	N	1
36	N	+	+	1	N	2	41.5	N	N	43	N	N	44	N	N	N	N	45.2	N	N
36	N	+	+	1	N	1	40	N	N	42.5	N	N	43.5	N	N	N	N	45	N	N
34.7	N	+	+	1	2	2	39.7	N	N	39.5	N	N	41	N	N	N	N	43	N	N
33	1	+	-	3	N	2	33.2	2	DD+	33.5	2	DD+	34	2	N	N	DD	34	2	5
35	N	+	+	1	N	1	39	N	N	39.5	N	N	41	N	N	N	N	42.8	N	N
34.6	N	+	-	2	N	2	38.7	N	N	37.5	2	DD+	38	2	squint +	N	DD	38.4	2	3
36	2	+	++	3	1	1	40	2	S	42.6	N	DD+	43.5	2	N	N	DD	45	2	4
36	N	+	-	2	N	1	36.2	N	N	39	2	N	41	N	N	N	N	42.5	N	1
35.5	1	+	-	3	1	1	36	1	DD	37	1	DD+	38	1	N	N	DD	39	1	4
35	N	+	+	1	N	1	41	N	N	43	N	N	44	N	N	N	N	45	N	N
34.6	N	+	+	2	N	1	40	N	N	42.7	N	N	44	N	N	N	N	45	N	N
35.6	N	+	-	1	1	2	40	N	S	42.8	N	DD	44	N	N	N	DD	44.7	N	2
35	N	+	+	1	N	1	37	N	N	40	N	N	42	N	N	N	N	43.8	N	4
35	1	-	-	3	2	1	40.5	2	DD	42	2	DD	43.5	2	N	N	DD	45	2	4
37	N	+	++	2	N	1	38	N	N	41	N	N	43.5	N	N	N	DD	45	N	1
37	N	+	+	1	N	1	39	N	N	41.5	N	S	43	N	N	N	N	44	N	N
35	1	-	-	2	1	1	39.6	1	DD	40.2	1	DD	41.5	1	N	N	DD	43	1	4
37	N	+	-	1	N	2	39	N	DD	42	N	DD	43.5	N	N	N	S	45	N	1
36	N	+	+	1	N	1	40.5	N	N	42	N	N	43	N	N	N	N	44.8	N	N
37	N	+	+	1	N	2	39	N	N	41.5	N	N	43	N	N	N	N	45	N	N
34	N	+	-	1	N	2	38.8	N	DD	40.5	N	DD	42	N	N	N	DD	44	N	3
34	N	+	+	1	3	2	38	N	N	41	N	N	43	N	N	N	N	45.2	N	N
35.5	N	+	+	1	N	1	39	N	N	41	N	N	43	N	N	N	N	44.7	N	N
32	N	+	-	2	N	1	33	N	N	34	N	N	36	N	squint +	N	S	38	N	2
35	N	+	+	1	N	1	40	N	N	42.5	N	N	44	N	N	N	N	45	N	2
38	N	+	+	1	N	2	40.6	N	N	42	N	N	46	N	N	N	N	47	N	N
35	N	+	-	1	N	1	38	N	N	40.8	N	S	41	N	N	N	DD	42.8	N	2
34.5	N	+	+	1	N	1	39	N	N	42	N	N	44	N	N	N	N	45	N	N
34.5	N	+	+	1	N	1	37	N	N	42.5	N	N	44	N	N	N	N	45	N	N
33	N	+	+	1	N	1	38	N	N	41	N	N	42.8	N	N	N	N	43.5	N	N
35.5	N	+	+	1	N	1	40	N	N	42.8	N	N	44	N	N	N	N	45.8	N	N
35	N	+	+	1	N	1	40.5	N	N	42.6	N	N	44	N	N	N	N	45.7	N	N
34	N	+	+	1	N	1	36	N	N	40	N	N	42	N	N	N	N	44	N	N

A - NAME

B – SEX

C – GRAVIDA

D – ANTENATAL RISK

E – PLACE OF DELIVERY

F- MODE OF DELIVERY

G-RESUSCITATION

H-NICU ADMISSION

I – NNC

J-VENTILATION

K-SHOCK

L -HYPOGLYCEMIA

M -MULTI ORGAN INJURY

N - SEPSIS

O - DIAGNOSIS

P - LENGTH

Q - WEIGHT

R - HC

S - TONE

T –NNR

U -DTR

V-NEUROIMAGING

W - VISION

X - HEARING

Y -HC 1 (3 MONTH)

Z -TONE 1 (3 MONTH)

AA - DDST 1 (3 MONTH)

AB -HC 2 (6 MONTH)

AC - TONE 2 (6 MONTH)

AD -DDST 2 (6 MONTH)

AE -HC 3 (9 MONTH)

AF- TONE 3(9 MONTH)

AG -VISION 2 (FOLLOW UP)

AH -HEARING 2 (FOLLOW UP)

AI -DDST 3(9 MONTH)

AJ -HC 4 (12 MONTH)

AK -TONE 4 (12 MONTH)

AL -DASII

KEY

SEX m- male, f- female

GRAVIDA 1- primi 2- multigravida

ANTENATAL RISK 1- meconium stained amniotic fluid 2- GDM 3-PIH

PLACE OF DELIVERY I – inborn O - outborn

MODE OF DELIVERY 1- normal vaginal delivery 2- assisted vaginal delivery 3 - lscs

RESUSCITATION 1- tactile stimulation 2 – bag and mask ventilation 3 - intubation

HC (first visit)

TONE N – normal 1 – hypotonia 2 - hypertonia

NEUROIMAGING 1- normal 2- mild HIE changes 3- severe HIE changes

VISION N – normal 1 – disc pallor 2- temporal pallor 3- ROP

HEARING 1- pass 2 – refer criteria

HC 1 (3 MONTH)

TONE 1 (3 MONTH) N – normal 1 – hypotonia 2 - hypertonia

DDST 1 (3 MONTH) N – normal S- suspect DD- developmental delay

HC 2 (6 MONTH)

TONE 2 (6 MONTH) N – normal 1 – hypotonia 2 - hypertonia

DDST 2 (6 MONTH) N – normal S- suspect DD- developmental delay

HC 3 (9 MONTH)

TONE 3(9 MONTH) N – normal 1 – hypotonia 2 - hypertonia

VISION 2 (FOLLOW UP) N-normal

HEARING 2 (FOLLOW UP) N- normal

DDST 3(9 MONTH) N – normal S- suspect DD- developmental delay

HC 4 (12 MONTH)

TONE 4 (12 MONTH) N – normal 1 – hypotonia 2 - hypertonia

DASII 1 – borderline DD 2 – mild DD 3- moderate DD 4 - severe DD 5 - profound DD

ABBREVIATIONS

HIE – Hypoxic Ischemic Encephalopathy

DASII – Developmental Assessment Scale for Indian Infants

DDST - Denver Development Screening Tool

VEP - Visual Evoked Potential

BERA – Brainstem Evoked Auditory Response

OAE - Oto Acoustic Emissions

DQ – Development quotient

AVD – Assisted vaginal delivery

BMV – Bag and mask ventilation

NNC – Neonatal convulsions

HC – Head circumference

AKI – Acute kidney injury

DTR – Deep tendon reflux

NNR - neonatal reflux

MAS – meconium aspiration syndrome

PIH – pregnancy induced hypertension

GDM – Gestational diabetes mellitus

MADURAI MEDICAL COLLEGE
MADURAI, TAMILNADU, INDIA -625 020
(Affiliated to The Tamilnadu Dr.MGR Medical University, Chennai, Tamil Nadu)

ETHICS COMMITTEE CERTIFICATE

Name of the Candidate	:	Dr.S.Durgadevi
Course	:	PG in MD., Paediatrics
Period of Study	:	2015 - 2018
College	:	MADURAI MEDICAL COLLEGE
Research Topic	:	Study of Neuro developmental outcome of infant with hypoxic ischemic encephalopathy
Ethical Committee as on	:	24.12.2016

The Ethics Committee, Madurai Medical College has decided to inform that your Research proposal is accepted.

Member Secretary Chairman Dean / Convenor

Prof Dr V Nagaraajan
M.D., MNAMS, D.M., Dsc.,(Neuro), Dsc (Hon)
CHAIRMAN
IEC - Madurai Medical College
Madurai

DEAN
Madurai Medical College

URKUND

Urkund Analysis Result

Analysed Document: DISSERTATION FINAL.docx (D31549401)
Submitted: 10/22/2017 9:14:00 PM
Submitted By: dr.durgadevi17@gmail.com
Significance: 2 %

Sources included in the report:

plag.docx (D30991772)
http://www.easymbbs.org/perinatal-asphyxia-cause-management-complications/

Instances where selected sources appear:

5

CERTIFICATE

This is to certify that this dissertation work titled **"A STUDY ON NEURODEVELOPMENTAL OUTCOME OF INFANTS WITH HYPOXIC ISCHEMIC ENCEPHALOPATHYAT GOVERNMENT RAJAJI HOSPITAL MADURAI"** of the candidate **Dr.DURGA DEVI S** with registration number **201517103** for the award of MD degree in Branch **VII- PAEDIATRIC MEDICINE**. I personally verified the urkund.com website for the purpose of plagiarism check. I found that the uploaded thesis file contains from introduction to conclusion pages and the result show 2 percentage of plagiarism in the dissertation.

Guide & Supervisor sign with seal

ஒப்புதல் படிவம்

எனது குழந்தையின் மூளை வளர்ச்சி மற்றும் வளர்ச்சிப் பருவத்தினை பரிசோதனை செய்து கொள்ளவும், டென்வர் (DDST) வளர்ச்சி பரிசோதனை மற்றும் (DASII) வளர்ச்சி பரிசோதனை செய்து கொள்ளவும் சம்மதம்.

பெற்றோர் கையொப்பம்